The Journal of the American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 104, NO. 6 CHICAGO, ILLINOIS FEBRUARY 9, 1935

EARLY CUTANEOUS CARCINOMA

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In practice, one sees not infrequently circumscribed epithelial new growths that in theory are difficult to classify. Some of them develop into carcinoma. I have interested myself in an attempt to determine which lesions have this potentiality, for it should be possible to identify carcinoma in its exceedingly early phases.

It is plain that a new growth which has appeared where previously there was no growth must, while now obvious, have been at one time borderline, before that invisible, and before that nonextant. The argument bears no controversy that a lesion having arisen de novo must have had a beginning and must have progressively evolved.

The problem arises, At what point is a carcinoma not a carcinoma? At what point does a process appearing de novo attain the status of cancerousness?

I am of the decided opinion that, at least in many instances, it is correct to think that cancer is cancer from the start. The concept of carcinoma developing from a "degenerated verruca," or from a "precancerous keratosis," is to my mind vague, indecisive, unclear and not representative of the truth.

It is common experience that abnormal aggregates of cells do de novo become clinically apparent, do progress over periods of weeks, months or years, do increase volumetrically, in two dimensions of surface and one of thickness, and do ulcerate and enlarge and cause by their presence and activity of growth deleterious effects in their host.

A., a man, aged 60, had a raised, rounded, crusted lesion 1 cm. in diameter and from 3 to 4 mm. thick on the skin of the left preauricular region. One year previously there was no lesion of any kind to the best of his knowledge. A small "freckle" appeared, scaled off and seemed to be gone, later recurred, and attracted his attention six months before. It had enlarged rapidly in the past month, crusting and bleeding when the crust was removed. Excised with the actual cautery, this tumor was composed of a mass of irregular, multinuclear and polymorphous epithelial cells that underwent atypical keratinization, and it was diagnosed squamous cell carcinoma.

I quote this one instance in substantiation of the thesis that cancerous lesions come into existence on sites previously normal, a fact of common experience.

The next problem is to establish cases of indubitable carcinoma, to examine new growths of a less advanced stage, and to show that they are of the same nature but simply less advanced and that they differ not qualitatively but quantitatively. I agree with Broders [1] that "the entity called carcinoma, regardless of etiology, is a primary disease of epithelial cells, and all other phases and sequelae, though of great importance, are in reality of secondary nature." The clinical entity called carcinoma, I consider fundamentally a colony or culture of abnormal epithelial cells growing parasitically on a host. I therefore make the assumption that a carcinoma is a carcinoma independently of its size. This is a reasonable biologic assumption; analogously, a solitary fertilized ovum is as truly an individual living entity as is the adult into which it grows.

The difficulty in studying what might be called embryo specimens of carcinoma lies in the fact that one never excises a portion of a lesion, allows a part to incubate on the host, and removes additional bits from time to time until a full blown, uncontrollable cancer has evolved from the remainder. Such an experiment is easily conceived, and it would yield specimens showing indubitable steps in progress. But, if it should be done, while it might indicate the steps of continuous evolution of a carcinoma, yet objection would be based on the effect of traumatism and inflammation on a lesion that might otherwise not have taken such a course.

The material from which one is forced to derive one's concepts, therefore, is not so fortunately consecutive as is ordinary embryologic material. Lesions that one arranges as consecutive stages come from different individuals at different times, and a series composed of them suffers from the objection that it is not an unbroken series. This is unfortunate, but there is no other way. If one can show that cases of circumscribed epithelial tumors, arising in different individuals, nevertheless possess characteristics that vary only in quantity and hence presumably only in duration, rate of progression or stage of progress, one will have satisfied oneself that they represent the same thing.

It is my custom, in treating a patient with what I believe to be an early carcinomatous lesion, to remove the entirety of it as a cylindric disk of dermis and epidermis, with a margin of normal tissue as narrow as I believe to be safe, by means of the actual cautery. The tissue removed is sectioned and the prepared slide examined to determine that the excision has gone beyond the margin of the atypical growth laterally as well as in depth. In no single case in my experience wherein the microscopic evidence has been clear that the tumor has been removed in toto has there been a recurrence.

Read before the Section on Dermatology and Syphilology at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 14, 1934.

1. Broders, A. C.: Carcinoma in Situ Contrasted with Benign Penetrating Epithelium, J. A. M. A. 99: 1670 (Nov. 12) 1932.

The material for this study has been furnished by specimens removed as described. On examining them microscopically, I have seen many intergradations between definite, advanced carcinoma and very early processes that appear to me to be simply less advanced lesions of identical basic nature.

It is to be kept in mind that, in every case I describe, I am limited by the human impossibility of knowing what the lesion would have developed into had it been left alone. As Heimann [2] says, "No one on earth is clairvoyant enough to select a given pigmented macule . . . and point with certainty to its epithelioma-tous future."

While the concept of a disease process should include its progression in time, the microscopic examination of a particular lesion is temporarily stationary. "Histologic pictures depict only a state; they show only coexistent features, not a chronologic sequence." [3] I am endeavoring histologically to show that the structure of certain early and small lesions is such that it is reasonable to presume that if they were merely allowed to continue proliferating they would attain the structure, dimensions and characteristics of what is generally considered carcinoma.

Fig. 1 (case 1).—Branched and budding tubular masses of neoplastic epithelium invade the lip to a depth of 4 mm. The stroma is composed of densely infiltrated round cells. The epithelial cells are large, keratinize abnormally and possess irregular nuclei. This is plainly carcinoma.

Case 1 (fig. 1).—A man, aged 77, had a scaly spot on the lower lip to the left of the midline for perhaps eight years, though he had stopped smoking a pipe twelve years before. The patch had slowly and continuously thickened, especially in the past year, and its rate of growth seemed progressively increasing. It was now a rough crusted plaque set in the lip tissue, raised only slightly, about 1.5 cm. across, oozing and bleeding when the crust was removed. It was sharply circumscribed and felt hard and firm; it seemed about 0.5 cm. thick. It was asymptomatic except for tenderness on pressure. It had received no treatment or traumatism. The regional lymphatics were not palpably enlarged.

The tumor was excised with a pointed cautery, and the whole lump was sectioned vertically through its middle. Sections stained with hematoxylin and eosin showed an epithelial tumor embedded in the lip tissue to a depth of 4 mm., in a stroma of densely infiltrated round cells. The tumor epithelium took its origin from the surface layer and grew down in cylindric masses. Near the surface some of the cylinders had a lumen that was partly filled with keratinized and desquamated cells. The appearance in vertical section was as of tubules cut longitudinally. About 2 mm. from the surface all the cylinders were solid, and they became convoluted with lateral buds, so that vertical sections did not follow the axis but cut some buds tangentially so that they appeared as horny pearls, and others so that they appeared as circular and oval islands. Many such islands contained concentric laminae of keratinized and desquamated cells. Some contained loosened cells that were almost homogeneous and eosinophilic. The external layer of cells of both the cylinders and the islands were more than normally variable in size; their outline was less sharply distinct, their nuclei varied in size, shape and uniformity of staining, and in keratinization they tended to retain their nuclei and cell outline, which varied in size and was frequently huge as compared with the normally keratinized epithelial cell of the nearby corneum. Around some of the cylinders and outbuddings that appeared like islands, the peripheral layer was seen to proliferate into the loose, cellular stroma in strands of thickness of only one or two cells.

The downward extent of the tumor mass into the loose, soft tissue of the lip was fairly sharply demarcated from the muscle fibers against which it had pushed. The border zone was narrow. While there was no capsule, the round cell infiltration, dense about the epithelial buds, left off sharply and was limited to the region only of epithelial growth.

The sections showed that normal tissue surrounded the tumor laterally and beneath.

This case is plainly carcinoma. Had the growth not been interrupted, the downgrowths would have continued. The abnormal mass would have enlarged, ulceration and sloughing would have occurred, and further increment in tumor quantity with attendant necrosis, infection and absorption would have led to the patient's death.

Case 2 (figs. 2 and 3).—A man, aged 59, was first aware of a "fever blister," which appeared on the lower lip about six months previously. This did not heal, and he continued to smoke with the pipe stem against the sore. The lesion had steadily and rather rapidly increased in diameter and thickness. It had been a crusting lesion from the start, but now the crust was more extensive, the lesion bled when the crust was forcibly removed, and it was tender and painful on pressure. The new growth was somewhat raised, fairly sharply circumscribed, firm to the touch, and set in the superficial portion of the lip like a whitish, lenticular disk with a granular, oozing surface. It was 11 mm. across and practically circular; it felt about 3 mm. thick in the central part, the edges being thin and continuous with the mucosa. It had received no treatment but had been injured slightly several times by the pipe stem. No regional lymphatics were palpable.

The tumor was excised with a margin of normal tissue by means of the pointed cautery and sectioned vertically through the middle. Microscopically, an epithelial proliferation was found embedded in the lip tissue to a depth of 2.8 mm. in a stroma of densely infiltrated round cells. The downgrowths were in such narrow cylinders and strands that the central portions of them had not keratinized, and only in some deeper aggregates had degeneration of centrally located epithelial cells occurred. There was, I presume, sufficient surface for nutrient exchange, so that within only the largest epithelial aggregates had keratinization occurred. Outbudding was so pronounced that a large proportion of the section showed epithelium in apparent islands. The surface from which the cylinders took their departure was covered by layers of epithelium of only one or two cells, and the stroma was not only densely infiltrated with round cells but contained many dilated capillaries engorged with blood, and many red blood cells were seen outside capillary walls. Many of the infiltrating leukocytes were polymorphonuclear, and the crust, composed of irregular and parakeratotic epithelial débris, was also purulent. In the larger epithelial aggregates within the tumor the cells were larger than normal, stained paler and were not regularly arranged. The peripheral layer was composed of lavender-staining cells that were variable in size, shape, chromatin content, and uniformity of staining. Round cells were seen interspersed between

2. Heimann, W. J.: Precancerous Dermatoses, J. Cancer Research 1: 343 (July) 1916.
3. Bloch, Bruno: Cancers and Precancerous Affections from the Dermatological Viewpoint, Cancer Rev. 7: 65 (Feb.) 1932.

the epithelial ones, and in the central portions of the largest aggregates irregularly cornified, eosinophilic degeneration products were found, constituting horny pearls and peculiar in being in many instances hollow and filled with leukocytes, and so constituting minute abscesses. The zone of epithelial growth limited the round cell infiltration, which, beneath the tumor, as in the preceding cases, was sharply demarcated from the

Fig. 2 (case 2).—The epithelial downgrowths reach a depth of 2.8 mm. in this circumscribed, crusted lesion of the lip. The zone of demarcation from deeper tissues is well defined. The stroma is like that of case 1 and case 3.

deeper lip tissue. At the margins of the tumor the downgrowths were shallow; at the central region they reached a depth of almost 3 mm., so that the lesion in the gross was lenticular.

The sections showed that the line of excision was well beyond tumor growth laterally and in depth.

I do not hesitate to call this carcinoma. It is clearly an infiltrative epithelial proliferation with microscopic and clinical evidence of active and atypical growth. In its probable further progression, had it not been interrupted, it is rationally presumed that it would have infiltrated deeper and more widely, ulcerated and sloughed, and produced a clinical picture completely reconcilable in all its attributes with the concept of carcinoma.

CASE 3 (figs. 4 and 5).—A man of about 65 had had a circumscribed, thin, asymptomatic scaly patch on the right side of the lower lip for about two years, which appeared insidiously and without attracting attention. It had slowly thickened and was now a firm, whitish, sharply marginated, scaling and crusting plaque, oval, about 5 by 6 mm. in surface, and it felt about 1 mm. thick. The central part was slightly thicker than the edge. It was not painful and had received no treatment. It was removed with the pointed cautery with a margin of normal tissue, and sectioned.

The sections showed epithelial tumor embedded in lip tissue to a depth of 1.1 mm. The epithelial downgrowths were roughly cylindric or ovoid, bulging, with rounded ends. They were not all alined perpendicular to the surface, so that some were cut axially and others at an angle. They filled the large proportion of the tumor area of the section. What stroma was present was composed of densely infiltrated round cells and capillaries engorged with blood. The epithelial downgrowths tended to branch and bulge. Their peripheral layer was not so regular as was the normal basal layer and in proliferation formed little buds about the blunt ends of the downgrowths. In places, these tended to loosen and extended out into the stroma. Within the aggregates of epithelium the cells were paler and larger than normal and tended in the larger aggregates to keratinize and form whorls. Such whorls in some places had become clear and distinct horny pearls, only 0.5 mm. from the surface. The zone of adjunction of tumor and deeper tissue was densely infiltrated with round cells, which were limited to the region of epithelial growth and demarcated it sharply from the subjacent tissue.

If this new growth had not been interrupted, it is reasonable to presume that the downgrowths would have extended. As their constituent cells multiplied in numbers, more outbuddings would have been produced, more horny pearls would have developed, and deeper invasion would have ensued. As the mass increased and the depth of invasion progressed, a picture resembling that of case 2 might reasonably be imagined to have evolved. Therefore, while this is an early and small lesion, it is my conviction that it is cancer.

CASE 4 (fig. 6).—A woman, aged 70, had a small, scaling dome-shaped, flattened, circular, reddish yellow papule 6 mm. in diameter located on the left cheek. It had been present not more than six months. It scaled slightly and itched a little at times. It was increasing in size steadily, she said. It felt about 1 mm. thick. It was removed with the pointed cautery and sectioned.

Microscopically, it was seen that the epithelium of 6 mm. of the surface was much thicker than normal; in actual measurement it reached a depth of 1 mm. Rounded papillary epithelial downgrowths extended into a stroma composed of densely infiltrated round cells and many capillaries. This infiltration was sharply limited to the zone of epithelial abnormality, and it sharply demarcated this from the deeper connective tissue. The whole process was limited to the superficial half of the dermis, and sebaceous and sudoriferous gland structures were found beneath the new growth, at a depth of 1.6 mm. from the surface. The downgrowing processes were somewhat looser in structure than those of case 3 and took more the form of strands than fat cylinders. The epithelial cells were separated a little more from one another, but the peripheral layer was equally irregular; the cells were also larger than those of the normal,

Fig. 3 (case 2).—The neoplastic cylinders are narrower and more branching. Their central keratinization in whorls produces horny pearls, and outbuddings are so pronounced that much of the epithelium appears as islands.

and the interior cells of the aggregates had likewise the tendency to undergo keratinization and to group themselves in whorls.

It is reasonable to believe that if this process had not been interrupted the downgrowths would have proliferated and extended deeper. As the aggregates increased in size, their central tendency to keratinize

and to form whorls would have manifested itself in the production of full-blown horny pearls. The branching outgrowths from the cylindric processes would have become more complex in configuration, so that sections would show apparent islands. The massive structure thus evolved would satisfy every criterion of true carcinoma.

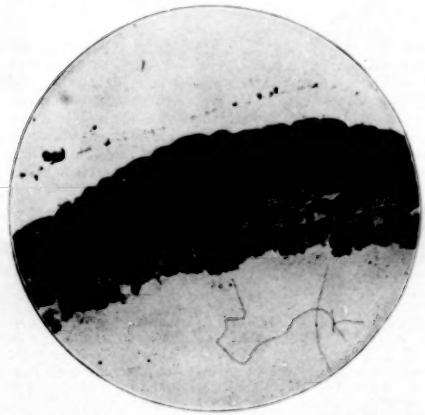

Fig. 4 (case 3).—Sections of this scaly plaque show broad downgrowths that branch a little. The depth of extent is quite sharply delineated, and the total thickness of tumor tissue is 1.1 mm.

This lesion might be called a senile keratosis. As Hookey [4] states, "the microscopic picture of keratoma senilis suggests the possibility of further evolutionary changes of malignant character." Eller and Ryan [5] observe that "when a senile keratosis becomes verrucous, it is a carcinoma." It is my opinion that case 4 is already carcinoma.

Malignancy, I believe, is a property of the tumor cell. The tumor mass, or clinical carcinoma, has no properties excepting those of its constituent elements. As Fraser [6] writes, "From the pathologic point of view, the cells in Bowen's lesion have already undergone the changes of malignant neoplasia, and for this reason the lesion should be classified as intra-epidermal carcinoma, not as precancerous." I believe that the cells of the lesions I have described are also already neoplastic.

A capacity for unrestrained growth and invasion can only be interpreted from, not observed in, any histologic preparation. It cannot by any human means be predicated as more than a presumption about any lesion that one sees, not imagines.

The lesions that I have presented have originated in the squamous layer of the epidermis. They are structures which, one may reasonably believe, would have evolved into gross carcinoma if not interrupted.

One must consider the present interpretation of precancerous lesions. The idea of a "precancerosis," a term first used by Dubreuilh in his thesis at the third International Dermatologic Congress at London in 1896, according to Bloch,[3] is commonly used to imply, among other lesions, some such lesions as I have described, particularly in cases 3 and 4. I believe that the differences between these cases are basically insignificant, and I have described them in accordance with this belief.

Definitions of "precanceroses" such as I am dealing with are vague. Cramer [7] says: "Precancerous is used in strictest sense as designating a condition which will develop into a malignant condition with a high degree of certainty." Sulzberger and Satenstein [8] define it thus: "The term precancerosis is a term which must be kept to designate conditions which, while not yet cancer, will, if untreated, practically invariably become cancer." Bloch's [3] careful review gives this definition: "We call precancerous those pathologic changes in tissue which, without being cancer, show the tendency sooner or later to develop into actual cancer." He calls this a "clinical-statistical" definition and bases it on two points: (1) the determination with mathematical certainty of the probability that a lesion will become cancer, and (2) the reaching of agreement on the percentage probability at which one is satisfied that a certain type of lesion is precancerous. That is, if 50 per cent of such lesions do become cancer, all such lesions may rightfully be considered precancerous. The concept remains unclear. Heimann [2] says: "The term 'precancerous dermatosis' has that alluring quality which captivates the imagination and courts acceptance until analysis reveals that it is inappropriate. At what point does precancerous lose its prefix? Is the problem one of medicine or etymology?"

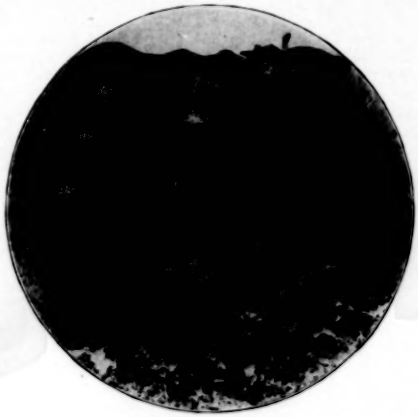

Fig. 5 (case 3).—Higher magnification shows the irregularity of the neoplastic cells, the tendency to keratinize in whorls, a horny pearl so formed, and a stroma quantitatively scant but qualitatively the same as in the preceding cases.

I have asked these questions, too. Bloch's definition is untenable. It makes a basic error in attempting to apply mathematics where mathematics is inapplicable. It is humanly impossible to determine the probability

4. Hookey, J. A.: Keratoma Senilis and Verruca Senilis, Arch. Dermat. & Syph. 23:946 (May) 1931.

5. Eller, J. J., and Ryan, V. J.: Senile Keratoses and Seborrheic Keratoses, Arch. Dermat. & Syph. 22:1043 (Dec.) 1930.

6. Fraser, J. F.: Bowen's and Paget's Disease of the Nipple, Arch. Dermat. & Syph. 18:809 (Dec.) 1928.

7. Cramer, W.: Brit. J. Dermat. 41:177, 1929.

8. Sulzberger, M. B., and Satenstein, D. L., Erythroplasia of Tueyrat, Arch. Dermat. & Syph. 28:798 (Dec.) 1933.

of a lesion's becoming cancer, for five reasons: 1. Either a lesion does become cancer, or it does not, so that a lesion is not statistically eligible. 2. If one examines the structure of a lesion, it is bottled in formaldehyde and has no biologic future. 3. If one has not determined the structure of the lesion and it becomes cancer, it is impossible to know what its structure was. 4. Before any lesion has become cancer, predictions about it are based on subjective, not objective, data, being based on presumption and not on perception. 5. After a lesion has become cancer, it is impossible to say when it was not cancer. If a lesion is interrupted, it has a structure either compatible with the possibility of being early cancer or not compatible, in which case it must be thought of as being either probably early cancer or probably not early cancer.

Bloch continues: "Of certain precanceroses, such as keratosis senilis, precancerous stage of xeroderma pigmentosa, of Bowen's and Paget, it may be said that in principle they always turn into cancer. Actually, however, the changes may occur so slowly that often the patient does not live the required number of years." Of this, I argue that, if the host is interrupted (e. g., by old age and death), and if the observer has the temerity to state that the lesion would have become cancer had the host lasted longer, the lesion must fall into the category of those which do become cancer and hence are cancer.

It is hopeless to attempt to decide at what percentage probability of becoming cancer a lesion may be called precancerous, because it is impossible to arrive at knowledge of this probability. Bloch admits that "reliable figures do not exist." I believe that such figures cannot exist. One must distinguish the connotations of "lesion" in the generic sense, such as senile keratoses in general, and "lesion" in the specific sense of this particular tumor on this particular patient. In the error of indiscrimination between these two meanings, the one collective and the other particular, lies the confusion of all statistical effort. Specific lesions not yet examined histologically are not yet diagnosed. Hence lesions collectively are not susceptible of a statistical assay with respect to their individual futures.

The concept that precancer is that which is not cancer but does become cancer is a concept not susceptible of scientific demonstration and outside the possibility of human proof.

One might define precanceroses as those lesions which may or may not be early cancer and cannot be decided on. Then one would be using the term "precancerosis" to designate a state of doubt as to whether the lesion is or is not early cancer. This is not a desirable usage. Bloch states that the concept of precancerosis is of practical importance because "the knowledge of precancerosis gives us the only means of practicing effective prophylaxis of cancer." This statement is erroneous, for, plainly, the effective prophylaxis of cancer depends on recognition of early and curable actual cancerous lesions, and on the knowledge of what may be early cancer. Nothing is gained by calling early cancer any other name, and any doubtful lesion ought as appropriately to be destroyed as a lesion regarding which there is no doubt.

One might define precanceroses as those lesions which are becoming cancer. But in such a definition the dividing line between precancer and cancer is implicitly admitted to be impossible. And precancer automatically becomes early carcinoma.

With the last possible meaning of "precancerosis" as, etymologically, rightly "that which precedes the earliest cancerous lesion," the precancer must be invisible. Should still earlier lesions come to light, precancer must still precede them.

Hence I am led to conclude that precancerosis has not been defined and cannot be defined; it is an idea,

Fig. 6 (case 4).—This dome-shaped dyskeratotic papule shows on section primary abnormality in the epithelium. The tendency to grow downward is evident. The cells tend to group and keratinize in whorls. The sizes of the cells and their nuclei are irregular. The cellular infiltrate is the same as that in the preceding cases. The total thickness of this very early carcinoma is 1 mm.

not an observable reality, and as a concept deserves recognition only as a confusing makeshift.

This removes the difficulty from the field of theory into that of practice. It may be hard to decide whether a lesion is or is not cancer. While the diagnosis may be, the lesion is not, on the fence.

The criteria of early carcinoma are difficult to arrive at. Broders [1] diagnoses his "carcinoma in situ" by the "altered cellular characteristics, in contradistinction to the cellular situation." Bloch states: "We know of no single macroscopical-clinical, or microscopical-histological change which is generally typical or pathognomonic. . . . " He lists:

(*a*) Proliferation and hypertrophy of epidermis, of irregular type.
(*b*) Unrest and irregularity of the whole epidermal structure.
(*c*) Increase of mitoses; irregular and pathologic mitotic figures.
(*d*) Polymorphism of cells, particularly of nuclei (giant, double and multiple, micronuclei, clumping of nuclei, etc).
(*e*) Dyskeratotic manifestations.

These features may be summarized as evidences of cellular malignancy or neoplastic alteration. Hansemann's [9] concept of "anaplasia," used to explain the origin of cancer cells, is not sufficiently specific in meaning. I am in agreement with the hypothesis of Whitman [10] that, in view of the atypical mitoses, multipolar divisions, hyperchromatic and hypochromatic

9. Hansemann, David: Virchows Arch. f. path. Anat. **119**: 229 (Feb. 4) 1890.
10. Whitman, R. C.: Somatic Mutations as a Factor in the Production of Cancer, J. Cancer Research **4**: 181 (April) 1919.

nuclei, asymmetric mitoses and changes in the number of chromosomes, the cancer cell is "a new kind of cell, strictly and literally a mutated cell." The earliest clinical cancerous lesion is then the smallest visible colony of progeny of a mutant somatic cell. The earliest theoretical cancerous lesion is the first mutant cell which, altered by mutation, retains its visibility, reproductive capacity and potentiality of being the ancestor of a parasitic colony, and loses its responsiveness to the host's control of its growth. One can imagine that a mutant may not be viable and so never produce a clinical lesion; the mutant may be partially controlled and so produce benign lesions, or there may occur many mutations within one atypical cell colony, resulting in a tumor with several kinds of cells in it, such as basosquamous lesions. With this hypothesis, a precancerosis might be understood to be a lesion in which neoplastic mutation is likely to occur. In the lesions I have described, however, it is my belief that the mutation has already occurred and that the status of cancerousness has already been attained.

CHARACTERISTICS OF EARLIEST RECOGNIZABLE SKIN CARCINOMA

On the basis of the foregoing considerations, I describe earliest recognizable skin carcinoma from three standpoints: the clinical, the microscopic and the theoretical. Clinically, they are circumscribed epithelial lesions that have arisen de novo, generally brownish, rough, scaly or verrucous in character, asymptomatic or slightly pruriginous, occurring by predilection on surfaces exposed to sunlight or irradiation, especially in persons with sun-sensitive skins. Microscopically, they manifest epithelial irregularity, acanthosis and dyskeratosis, with changes in cell type of the order of abnormal mitoses and atypical morphology, and with evidence of the probability of proliferative extension into a dermis that is characteristically infiltrated to a greater or less degree with round cells in the immediate region of epithelial abnormality. Theoretically, they are interpreted as colonies of progeny of mutant epidermal cells, with retained capacity for proliferation, and lost responsiveness to growth control on the part of the host.

Such a descripition is independent of the size of the lesion, in accordance with the theory that one cell can constitute a cancer. It is independent of rate of growth of the lesion, for the progression may be so slow as never to interfere with the well being of the host. It stresses the concept that carcinoma in the gross is purely a manifestation *en masse* of epithelium growing abnormally. It conceives relative malignancy as dependent on balance between proliferative capacity of tumor cells and resistance of the host. It explains multiplicity of cell type in one tumor on the basis of mutation following on mutation. It enlarges the concept of skin carcinoma, and it offers a reasonable and unified conceptual design for the interpretation of neoplastic processes. It is eminently practical, for it encourages suspicion of minute lesions, which might grow into gross carcinomas.

The therapeutic correlate is that, if a lesion may cause serious trouble later, now is the time for its destruction.

CONCLUSIONS

1. (*a*) Many skin cancers begin as de novo lesions.

(*b*) The earliest visible lesion in these cases is a circumscribed, scaly, epithelial new growth.

2. (*a*) The structure of many minute, scaly, epithelial new growths is such that it is reasonable to presume that, if not interrupted, they would become obvious carcinomas.

(*b*) It is reasonable to believe that such lesions are in fact early carcinomas.

(*c*) If a lesion has a structure not compatible with a likelihood of its being early carcinoma, it might be called precancerous. But it would be impossible to predict that such a lesion might develop a structure, if uninterrupted, such that it would be properly called carcinoma.

3. (*a*) It is impossible to determine at what point in its natural history a cancerous lesion was not cancerous.

(*b*) It is reasonable to believe that cancer is cancer from the start.

4. The concept of precancerosis is indecisive and undefinable. It groups unrelated conditions, which may or may not be early cancer. Its acceptance entails an insoluble problem of a dividing line between cancer and not-cancer, as well as an insoluble problem of statistical assay of lesions that are strictly individual.

5. (*a*) A lesion may be cancerous independently of its size and rate of growth.

(*b*) Cancer is primarily an epithelial disease.

(*c*) A cancer consists of mutated somatic cells.

(*d*) The earliest visible manifestations are circumscribed, dyskeratotic lesions which microscopically are composed of polymorphous epithelial cells that proliferate, keratinize and undergo mitosis in an abnormal manner.

(*e*) Malignancy depends on a balance between the proliferative capacities of its cells and the control or resistance of the host.

(*f*) One tumor may contain several kinds of cells as a result of mutation following on mutation.

6. Early cancerous lesions are readily destroyed and cured. In suspecting all early lesions and destroying them, one would prevent the development of all late lesions such as might become incurable.

801 Lathrop Building.

ABSTRACT OF DISCUSSION

DR. E. W. NETHERTON, Cleveland: To obtain the best results, the correct diagnosis must be established at the earliest possible stage. Early diagnosis followed by complete surgical removal is still one of the best methods of treating squamous cell carcinoma. This type of management makes possible a thorough histologic study of each lesion, which is essential if the benign and doubtful lesions are to be separated from those of early carcinoma. A statistical study of a large series of early cases which had been treated in this fashion with observation of the patients over a period of years would be of considerable value. What is especially needed is some criterion by which the benign and early malignant epithelial new growths can be differentiated by their gross morphologic characteristics. In many instances the microscopic examination does not give conclusive results. The greatest difficulty is encountered in the borderline cases, and it is not unusual for equally clever pathologists to differ in their interpretation of the clinical and microscopic observations. The term "precancerous" has been used for years to designate the malignant potentiality of lesions such as leukoplakia, senile keratosis and xeroderma pigmentosum. Dr. Sutton has given many good reasons why the concept of precancerosis is indecisive and undefinable. It is impossible to determine the future of any benign epithelial growth; nevertheless the conditions that have been designated as precancerous will in a high proportion of instances become malignant, but since nothing is known concerning the specific etiology of can-

cers there is no way of telling which apparently benign lesions will become malignant. It is difficult for me to agree that a senile keratosis, a leukoplakia, or a melanotic mole that has been present for years and has become malignant, was in reality cancerous from the start. Paget's disease of the breast and Bowen's keratosis by pathologic evidence have been shown to begin as cancerous lesions, but this is not the case with other types of so-called precancerous dermatoses. Precancerous is a poor term, but usage has established it firmly in medical nomenclature. If in its strictest meaning "precancerous" denotes that the lesion will invariably become malignant if its course is uninterrupted, it should be discarded, for, as Dr. Sutton has stated, such a statement concerning any particular lesion cannot be verified. However, if precancerous means that a certain lesion is potentially malignant and that it is probable that it will become malignant, I can see no objection to its use. It would be better to designate such lesions as potentially malignant. What is most important is that all early and potentially malignant lesions be recognized and removed or destroyed.

DR. HAROLD N. COLE, Cleveland: I have had the opportunity of looking over Dr. Sutton's histologic material. I know that he has painstakingly made serial sections on dozens of new growths, attempting to come to some conclusion on the argument advanced by Broders of a carcinoma de novo: of its being a carcinoma from the beginning. It is only by such studies that some conclusion can really be reached as to when a malignant condition starts or whether it does actually start from the beginning, or whether some of the lesions are going to remain precancerous and continue the same.

DR. JEFFREY MICHAEL, Houston, Texas: I have tried to study as many biopsies as possible of these early lesions. It all comes down to a question of a pathologic concept and a definition. If a cancer is defined as a tumor that must have invasive qualities, one cannot call these early lesions malignant. But if Broders' contention is accepted that there is such a condition as an epithelioma in situ which can be differentiated by certain cytologic changes in the cells, one should accept these changes as cancer from the beginning. I think that the old pathologic concept of invasive qualities being absolutely essential to a diagnosis of malignancy is being broken down in two directions: in the first, in the conception of Jadassohn and Borset that there is an intra-epidermal epithelioma, and in the second place in the conception of Broders that there is such a thing as epithelioma in situ.

DR. RICHARD L. SUTTON JR., Kansas City, Mo.: The arguments that I wished to present are not nearly complete. The idea that cancer in order to be called such must be an invasive lesion is to my mind not essential. A cancer is a structure composed of a number of cells of originally epithelial origin, which represent a true mutation from an orginally presumably normal somatic cell. That is the idea of Whitman, whom I have quoted. Cancer cells in general have been shown to vary in their cytology, in their number of chromosomes; and so the alterations that take place within them are those of true mutation in the biologic sense. They have fewer or more chromosomes than normal, and their progeny have atypical divisions. In my opinion, one cell that retained its capacity to proliferate but lost its capacity for being controlled by the host on which it was proliferating would constitute a cancer. Certainly one melanocarcinoma cell in a capillary in the liver would constitute a cancer in the sense that such a metastasis produces a separate colony of living cells capable of proliferating there and doing further damage. One sees these peculiar cells in situ. All one has to do is to examine lesions in order to find them. Broders has pointed them out in numerous instances, and in looking over many sections I have seen them too. I imagine that they represent somatic mutations and so colonies of mutant cells that have the capacity for invasion. The word "malignancy" has so many different meanings that it is hard to know just how to apply it to this concept of cancer. One can't tell whether the cells of a lesion are proliferating or whether they are invading; one can't see them acting, because as soon as one looks at them microscopically one has killed them; they are in formaldehyde. So it is a mixture of clinical and microscopic evidence from which one must derive one's concepts.

BORDERLINE BREAST TUMORS

BIOPSY AND POSTBIOPSY TREATMENT

JOSEPH COLT BLOODGOOD, M.D.
BALTIMORE

There is still a good deal of difference of opinion among those best informed as to the type and method of biopsy and as to prebiopsy and postbiopsy irradiation in breast tumors.

I have been observing the results in all breast tumors in which the tumor has been explored first. The object of this exploration was to determine its pathologic nature. Up to 1915 in the Halsted Clinic at Johns Hopkins, the naked-eye diagnosis had been depended on. In my own experience since 1915 I have used naked-eye diagnosis in every case, but, in addition, an immediate frozen section for microscopic study was resorted to in the operating room, and the operation or treatment that followed rested largely on the diagnosis made on this immediate frozen section.

Great changes have been observed and recorded by me since the first exploration that I witnessed on a borderline breast tumor more than forty-two years ago.

These changes have been forced on the operator and his surgical pathologist by the decreasing preoperative incidence of malignant tumors in the clinic and the increasing occurrence of benign and borderline tumors. In the last five years, borderline tumors in which it is difficult to determine whether they are malignant or benign have greatly increased in numbers.

In the first fifteen or twenty years of the Halsted Clinic more than 98 per cent of the women complaining of breast lesions had definite lumps in the breast and were subjected to immediate operation. In fully 80 per cent of these cases the tumor proved to be malignant. In my own clinic today only 15 per cent, instead of 98 per cent, are subjected to operation, and the incidence of cancer in the total number is less than 10 per cent, and the incidence of malignant tumors in those subjected to operation is less than one half. The pathologic type of the distinctly palpable breast tumor subjected to exploration which has shown the greatest increase in the past three years is the borderline breast tumor, which I [1] described in detail in a paper published in 1932. There are fifty-eight illustrations in that paper, and since the date of its publication two and one-half years ago, the number of new cases has been equivalent to what I had previously observed in twenty years.

METHOD OF BIOPSY IN DOUBTFUL CASES

The method of biopsy is employed when the palpable mass is small enough to be excised with a good margin of uninvolved breast tissue and the wound closed without producing loss of symmetry in the breast. In these cases the gross and microscopic appearance of the tumor is not seen until the tumor is bisected, when held in the hollow of the left hand of the operator, studied with the naked eye and an immediate frozen section made and examined. If the operator and his pathologist are confident that the tumor is distinctly benign, the wound in the breast is closed and no postoperative irradiation is employed. When the operator and his pathologist are confident, from the gross

Read before the Section on Surgery, General and Abdominal, at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 14, 1934.

1. Bloodgood, J. C.: Am. J. Cancer **16**: 103 (Jan.) 1932.

appearance and the frozen section, that the tumor is distinctly malignant, an alcohol sponge or a gauze sponge saturated with a 50 per cent solution of zinc chloride (and squeezed dry) is placed in the wound, the skin sutured over it and the complete operation for cancer performed at once.

These two procedures for tumors of the breast, when there is no doubt about their pathologic nature, have been accepted by the majority of operators, pathologists and radiotherapists. I am beginning to accumulate evidence which clearly indicates that there is no danger in closing the wound, without either the alcohol or the zinc chloride sponge after the removal of the malignant tumor, and in subjecting the patients to postbiopsy irradiation. I am beginning to accumulate evidence that, when the malignant tumor is smaller than a twenty-five cent piece (24 mm.) and has been present one month or less, its local excision and postoperative irradiation may offer as many chances of a permanent cure as the radical operation. In a number of such cases of which I have records, operation has been done in this way (in other clinics and in a few in my own clinic) when the patients refused the complete operation.

Fig. 1.—Appearance of patient about one year after the excision of a clinically benign, but microscopically doubtful or borderline, breast tumor removed during the early months of pregnancy. The circle in ink on the forearm represents the palpable subcutaneous tumor that was removed June 13, 1932, under procaine hydrochloride and proved to be a benign nerve-sheath tumor. This patient was free from a recurrence of either tumor in July 1934, two years and some months after the operation on the breast.

The third type of breast tumor is that in which the operator and his pathologist are in doubt as to a malignant condition. This is the true borderline tumor. From my study of borderline tumors since 1892 I have found, with the rarest exceptions, that they are benign. If the complete operation is performed immediately or later, the axillary glands show no metastasis. Practically all patients with such borderline tumors have been followed from five to forty-two years. In not a single case up to the time of death, or at the present time if the patient is living, has there been any sign of malignancy in the scar or of internal metastasis. The percentage of malignant involvement of the other breast has been identical with that in an equal number of benign adenomas of the breast at the same age and followed through the same periods of time.

There seems to be largely an agreement among the greatest authorities as to this method of biopsy when exploration must be done to determine the pathologic type of the tumor and when the tumor is sufficiently small to allow its excision through uninvolved breast tissue and the closure of the defect in the breast without producing loss of symmetry.

To repeat, the majority of expert authorities urgently advise the immediate complete operation should the operator and his pathologist decide that the lesion is distinctly malignant. Of course, they all agree to the restricted removal of the tumor of the breast only when it is agreed that it is benign.

There is a great difference of opinion as to the method of procedure in the borderline tumor. I am advising the treatment of the borderline tumor on the operating table as one treats the benign tumor, but, after the operation I advise irradiation of the breast and axilla while sections are being submitted to two or more widely experienced surgical pathologists.

In many instances this biopsy can be done under local anesthesia. If the operator plans to perform the complete operation, should the tumor prove to be malignant, he should work in the operating room of a hospital with full preparation for the complete operation. When the operator who has had experiences similar to mine and feels justified in closing the wound no matter what the nature of the tumor may be, and give irradiation first even if the complete operation is to be done later, it is not essential that the patient be prepared for the complete operation.

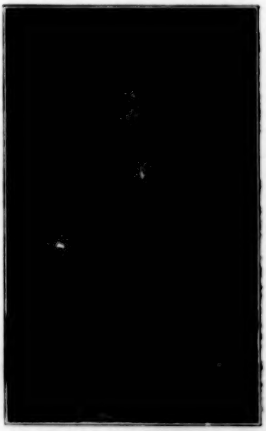

Fig. 2.—Appearance of a bisected tumor from the breast of the patient shown in figure 1.

There is no question that the education of women has increased the number coming to the clinic with benign conditions of the breast for which operation is not indicated. Also there is no doubt that transillumination in a dark room, as first advocated by Dr. Max Cutler of Chicago, has done more than any other new procedure for the distinct recognition of a benign blue-domed cyst larger than a twenty-five cent piece. In my clinic we no longer subject to operation distinctly palpable tumors larger than a twenty-five cent piece unless they transilluminate dark.

There is a fourth group of tumors that are increasing in numbers with the exploration and complete excision of clinically benign tumors of the breast. These

tumors are solid and have the distinct gross and microscopic appearance not only of a malignant growth but of a grade IV acute carcinoma; that is, the type of tumor which, if neglected by the host, develops ultimately into cancer *en cuirasse*. My entire experience teaches me that in every stage of its development this grade IV acute carcinoma is best not subjected to operation. So far they have never been cured, but the

Fig. 3.—Section showing nonencapsulated tumor removed during early months of pregnancy from patient shown in figure 1. This section was taken from the center of the tumor, showing stroma of the old adenoma and definite gravidity hypertrophy of the parenchyma.

duration of life is often prolonged and the patient made distinctly more comfortable by proper irradiation without the complete operation, even when the tumor is observed in an inoperable stage or is recognized with the microscope in a frozen section at the exploratory biopsy for an apparently benign tumor of the breast.

One has to bear in mind that the actual change in the relative number of malignant breast tumors which are still clinically benign and must be explored is toward an increase. I am convinced of this because it has been shown in excised breast lumps sent to me for examination. The women of this country are showing the results of the educational efforts of the American Society for the Control of Cancer, the medical societies, and individuals in the medical profession. When 80 per cent of distinct breast lumps are cancer and more than 95 per cent of these are evidently so clinically, exploration for a malignant tumor is the exception rather than the rule. In many hospitals today there is an increasing number of breast tumors explored in the operating room, an increasing number submitted to frozen section in the operating room, and an increasing number in which the pathologist is in doubt as to the diagnosis. The pathologist must be able to advise this group what to do in case of doubt. In fact, in the most experienced clinics in the world today the number of borderline tumors found at exploratory biopsy is on the increase. Every surgeon and his pathologist know what to do when the breast tumor is distinctly benign, and they still know what to do if they wish to follow the major opinion when the breast lump is distinctly malignant. Very quickly the educated community will force on the operating surgeon and his pathologist an increasing number of borderline tumors.

In my opinion, the proper procedure is the complete excision of the palpable lump, by cutting through uninvolved breast tissue, by closing the wound and by giving postoperative irradiation to the breast and axilla.

There is a difference of opinion among radiotherapists as to the time that should elapse before the closed wound in the breast is irradiated. There is no doubt that if begun at once the wound may break down, and if this wound becomes infected, it interferes with the value of irradiation. I am advising the irradiation at once when the frozen section favors an ultimate diagnosis of malignancy and have advised delay when the section favors a benign condition. By great care of the wound, should it break down, infection can be avoided. In view of the fact that there is such a difference in ability among even well trained surgical pathologists to recognize the malignant tumors of the breast in their earliest stages, I am inclined to the view that it may be safer to give irradiation over the axilla at once, protecting the breast wound and giving irradiation over the breast and its wound within a week or ten days. In three cases subjected to immediate irradiation the wound broke down but did not become

Fig. 4.—Periphery of tumor shown in figure 3. A typical hypertrophy of the parenchyma.

infected and healed perfectly by granulation. In many instances the wound did not break down. So far I have observed no bad results from irradiation.

SECOND TYPE OF EXPLORATORY BIOPSY OF BREAST TUMORS

Halsted, beginning in 1889, in his clinic at Johns Hopkins, when he explored a breast tumor cut directly down into it with the knife, and, if its naked-eye appearance suggested to him a malignant growth, he

cauterized the cut tissue with phenol (carbolic acid) followed by alcohol, closed the wound, changed instruments and towels, and performed the complete operation for cancer. Such explorations were of rare occurrence, and the patients were most carefully followed. We could never find evidence that this exploration followed at once by the complete operation decreased the chances of a permanent cure. When the glands were not involved, 70 per cent of the patients were living at the end of five years, whether there had been an exploration or not. In the majority of breast tumors explored, the glands were not involved. When the glands were involved, the five-year cures did not seem to be affected by an exploratory incision followed at once by the complete operation.

Fig. 5.—Areas of tumor shown in figure 3, which many pathologists diagnosed malignant, many benign.

Halsted was so confident of his naked-eye diagnosis that he was very late in adopting frozen sections. I have only one positive case in which Halsted failed to recognize a malignant condition by the naked-eye appearance of a breast tumor and restricted his operation to the removal of the tumor only. The tumor was a smooth-walled and thick-walled cyst containing blood. There was no papilloma. Cancer was not recognized in the wall until permanent sections were studied within one week. The complete operation was then performed, and the removed glands in the axilla and above the clavicle showed metastasis. The patient died of internal metastasis. In a letter to Dr. Welch, written some two years before Dr. Halsted died, he expressed great satisfaction over his ability to recognize with the naked eye the correct pathologic condition of tissue exposed at operation.

Another evidence of this extraordinary ability of Dr. Halsted is the borderline tumors he explored up to 1915. In not a single instance did he look on this nonencapsulated tumor as malignant. After cutting into it he excised it as he would an encapsulated benign tumor or a blue-domed cyst. He closed the wound without performing the complete operation. The tumors were then sent to the laboratory. In the early years they were diagnosed adenocarcinoma by Dr. Welch. After 1892 they were diagnosed by myself, usually in consultation with Dr. Welch. Dr. Halsted accepted the microscopic report of malignancy and performed the complete operation. As I have already said, the axillary glands were never involved, and these patients lived for years and before or at death showed no signs of cancer. In 1915 I submitted the section from these borderline tumors to a large number of the best trained surgical pathologists in New York, Philadelphia and Detroit. The written diagnosis of the majority was malignancy, or suspicion of malignancy. There was never a unanimous vote in favor of malignancy. There was always a minority in favor of a benign condition. Many of these cases have already been reported.[1] These identical sections have been again referred to a group of pathologists and surgical pathologists who attended the microscopic diagnostic demonstrations in the Surgical Pathological Laboratory of the Johns Hopkins Hospital in the last four years. In every instance there is still a difference of opinion, but the larger number vote benign, while in 1915 the majority voted malignant. Sections from malignant tumors of the breast submitted to these groups are always diagnosed without exception malignant. Therefore, when two or more pathologists of average training and ability differ as to the malignancy of a breast tumor, the chances are that it is benign and will be cured without a more extensive measure than the removal of the tumor only.

These borderline tumors are on the increase. The present paper is designed to call attention to the fact that when the tumors are small enough the method first followed by Halsted should be changed to the complete removal by cutting through uninvolved breast tissue. But when they are too large for this method they may be cut into. The encapsulated solid tumor must be differentiated by frozen section, because often in young and in older women the larger tumor may be a fibroadenoma or a sarcoma. In the benign tumor the breast can be saved. In the malignant tumor the breast and the major pectoral muscle must be completely removed. The direct incision into breast tumors is necessary now

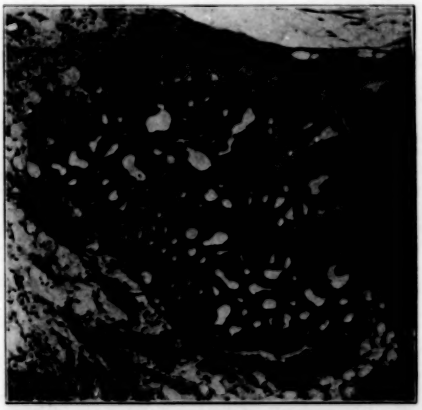

Fig. 6.—Section of the normal breast in pregnancy removed with the tumor shown in figure 2.

in far fewer cases; more often is the gross pathologic appearance of a blue-domed cyst or a distinctly encapsulated tumor so obvious that a frozen section is only confirmatory of the naked-eye appearance.

I will reproduce here the illustrations of two cases that represent two distinct clinical types: One was clinically benign, a case in which the tumor was excised by cutting through normal breast, the seat of pregnancy hypertrophy. There was a difference of opinion on the frozen section at the time of the operation, and for this reason the patient was given immediate irradiation over the axilla without irradiation of the wound. There has been a difference of opinion on the interpretation of the sections among my own associates and at every meeting for the microscopic demonstrations held at the Surgical Pathological Laboratory of the Johns Hopkins Hospital since. This patient has been well now more than two years and has had a second pregnancy and normal delivery. During the second pregnancy four or five nodules appeared above the scar in the breast. These were not skin metastases but little breast tumors from 2 to 5 mm. in diameter. They disappeared temporarily after the birth of the child. The child was weaned and then, when the menses appeared, the tumors returned for a few weeks and disappeared again.

This patient (fig. 1) has no sign of any disease in either breast or other part of the body today, in spite of which there is a minority in my own laboratory who still interpret the microscopic sections as malignant, and the majority of those who restudied these sections during the microscopic demonstrations held three times a year still cling to the diagnosis of malignancy. One of the special workers in the laboratory has reviewed most thoroughly all the tumors of the breast removed during pregnancy and during lactation and compared them with this case. He is still of the opinion that this case must be interpreted as malignant in spite of the fact that the patient is well more than two years after the removal of the tumor only and irradiation of the axilla only.

In spite of their larger experience with these borderline tumors, the best pathologists still disagree, but when they do so the patients live. Therefore, if good pathologists disagree it is fair to the patients to restrict the operation to the removal of the tumor. There is no objection to irradiating the axilla and protecting the wound of the breast while the decision of the pathologists is being awaited, and there is no objection—if there is disagreement—to finish the course of irradiation over the breast. I myself was so convinced that this case was pregnancy hypertrophy that I gave no more irradiation. I stopped her nursing after both pregnancies in order not to excite further growth in other areas of benign adenoma of the breast.

Figure 1 was taken about one year after the birth of the child when all examinations were negative, except a small tumor, outlined in ink, on the forearm, which was removed in June 1932 and proved to be a benign nerve sheath tumor. Later, with the second pregnancy, as already reported, nodules appeared in the periphery of the breast above the scar.

Figure 2 shows the good margin of uninvolved breast tissue in pregnancy hypertrophy removed with a central zone of nonencapsulated tumor tissue. The tumor tissue is smooth, while the breast is faintly lobulated and projects above.

I felt this tumor in the patient's breast two years before her marriage. It was freely movable and about the size of a five cent piece (21 mm.). I advised its removal because of the danger of its giving her trouble if she became pregnant and warned her of the danger of losing her breast should she have this tumor removed during pregnancy or lactation, because many pathologists would diagnose it cancer. She had a second, smaller, tumor in the left breast, which disappeared before she was married.

Figure 3 is a microscopic section from the center of the tumor removed. It shows the increased fibrous stroma of the old fibro-adenoma and tremendous cell proliferation of the lobule of the old fibro-adenoma.

Figure 4 shows a section from the junction of the old fibro-adenoma and the breast, the seat of pregnancy hypertrophy.

Figure 5 is an area in the fibro-adenoma which influences many pathologists to the diagnosis of malig-

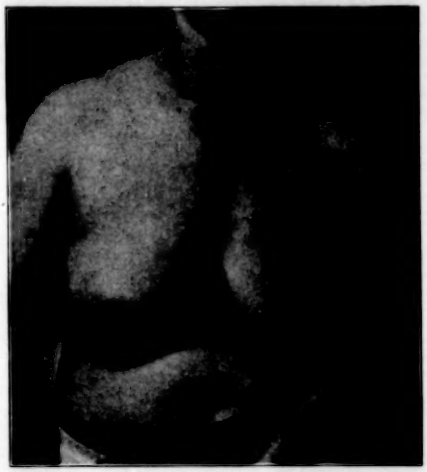

Fig. 7 (case 2).—Breast suggestive of malignancy; retraction of nipple shown is intermittent, favoring benignancy.

nancy, especially when they compare it with figure 6, which is a section of the normal hypertrophy of pregnancy.

I have been familiar with these typical microscopic pictures in distinctly encapsulated tumors removed from the breast during pregnancy or lactation. In not a single instance have I been able to find pictures in these lactating adenomas that resembled the microscopic picture of cancer in the breast during pregnancy or lactation. In practically all malignant tumors during pregnancy or lactation the axillary glands have been involved, and in more than 75 per cent in which the glands were involved the patients died of cancer. Billroth has called attention to the fact that adenomas of the breast are subject to the same changes as is the breast during pregnancy and lactation. But there is no complete study yet published with proper illustrations on the microscopic pictures of breast tumors during pregnancy and lactation, and of their differentiation from malignant tumors.

I have no evidence that malignant tumors in the breast during pregnancy or lactation arise in preexisting adenomas of any type.

The second case to be reproduced here (figs. 7 and 8) was a diffuse tumor of the upper hemisphere of the right breast, too large for complete excision. It was partially removed, numerous frozen sections were made, and the operator, my associate Dr. L. Clarence Cohn, decided that it was benign and saved the breast. There was no postoperative irradiation. There was a difference of opinion during the operation and has been since. It has now been more than three and one-half years; the patient is well, and the breast palpates and transilluminates normally. During this period I have been making in the laboratory a complete restudy of a type of breast tumor that I have called comedo-adenocarcinoma

Fig. 8.—Section of tumor in breast shown in figure 7, interpreted as benign comedo-adenoma by the operator. Incomplete removal. No recurrence in the remaining breast three and one-half years later. No irradiation before or after operation. In the upper half are typical comedones; the lower half of the picture shows intraductal papillary adenoma. No evidence of cancer.

and now call comedo-adenoma. When this tumor is of a pure microscopic type there has never been metastasis to the axilla, never death from cancer. But this comedo-adenoma may be associated with fully developed cancer, and then it acts like fully developed cancer with the same prognosis. The case shown in figures 7 and 8 is, under the microscope, the benign type of comedo-adenoma. I shall show only one microscopic picture here (fig. 8), because I expect to report fully on this case later in the *American Journal of Cancer*, as I delivered a paper on this subject before the American Society for Cancer Research in Toronto in May.

Figure 7 pictures clinically Dr. Cohn's case. The patient was a woman at the cancer age, and there were certain things in the clinical picture that made Dr. Cohn suspicious of a malignant growth, and for this reason he explored. The retraction of the nipple shown in the photograph was intermittent. The mass occupying the upper hemisphere of the breast varied in size. The patient was certain of this. When Dr. Cohn explored the tumor it was solid, diffuse and without cysts, but there were numerous comedos of granular débris which could be expressed from the surface of the tumor everywhere. There was no gross evidence of cancer—only comedo-adenoma. Nor, in the section (fig. 8) was there evidence of anything but comedo-adenoma, or what is known in the literature as duct cancer.

I urge every one who reads this article to read also a paper by Campbell [2] on chronic cystic mastitis. Campbell gives the best discussion of all the literature on the subject. There is also a splendid review of the early literature on chronic cystic mastitis by my associate Dr. Charles F. Geschickter.[3] The difficulty in presenting borderline tumors is, first, space for illustrations and, secondly, one must wait at least two or three years to ascertain the result.

The only way for surgical pathologists to become familiar with this group so difficult to diagnose is to study the microscopic sections repeatedly as the patient is followed.

My experience to date seems to justify my making the statement that when a surgeon operates on a clinically benign tumor that is small enough he should excise the tumor by cutting through healthy tissue and then, after its removal, bisect it in his hand and make frozen sections. If in doubt as to a malignant condition, the wound should be closed. If high voltage roentgen therapy is available, radiation over the axilla should be done. If the pathologic reports from a number of pathologists come in uniformly that the tumor is benign, or by the majority that it is benign, nothing further should be done. If the pathologists agree as to malignancy, or only the majority of them, there are two courses—either finish a thorough preoperative course of irradiation and then wait the proper time and perform the complete operation for cancer, or stop irradiation, wait a proper interval and then perform the complete operation for cancer. At the present time the majority of the best trained and experienced surgeons, pathologists and radiotherapists are of the opinion that complete operation for cancer should be performed on the doubtful breast tumor as soon as the pathologic report of the consulting group is received agreeing with, or with a majority opinion in favor of, malignancy.

My own opinion at the present moment, I appreciate, is a minority opinion. But I am gathering evidence in its favor and I propose to put this evidence before my colleagues as quickly as possible. I have sufficient evidence, however, to justify this conservative advice about borderline tumors, especially those of the type that can be excised completely as illustrated in the case in figures 1 and 2. In cases of the type of the second case illustrated in figures 7 and 8, the conservative operation should be reserved for those special clinics which have had large experience in the treatment of borderline tumors of the breast; otherwise, the complete operation for cancer of the breast should be performed at one sitting.

3301 North Charles Street.

2. Campbell, O. J.: Relationship Between Cystic Disease of the Breast and Carcinoma, Arch. Surg. **28**:1001 (June) 1934.
3. Geschickter, C. F.: Bull. Inst. Hist. Med. **2**: 249, 1934, in Bull. Johns Hopkins Hosp., June 1934.

ABSTRACT OF DISCUSSION

DR. IRVIN ABELL, Louisville, Ky.: More tumors requiring biopsy are being seen than ever before. I have used biopsy with immediate examination of the frozen tissue sections since 1917, feeling that the interpretation of the pathologist with the microscope would be superior to one's own naked eye interpretation, regardless of how much one correlates the experience of the two. When the biopsy proves the tumor malignant, my routine practice has been to close the wound and immediately proceed with a radical mastectomy. I am aware that in some quarters there is a disposition to vary from this treatment; namely, that when the tumor is small and is removed by biopsy and proved to be malignant, it may be treated safely with radium or x-rays. I have had no experience with this treatment but I have had come into my service five patients who have been so treated elsewhere: a small tumor was removed and radium was implanted in the wound, with subsequent irradiation after the healing of the wound. All five had recurrences in the breast and three had axillary metastasis. The result of complete mastectomy in the presence of a malignant condition has been so excellent as to compensate for the loss of the breast. The retention of the breast in the presence of a known malignant condition, to be treated subsequently with radiation, is fraught with danger, particularly if the practice becomes general. The wide variation in equipment, in technic, in dosage of irradiation, is such that it is a difficult matter for one to draw correct conclusions as to the evaluation of the method. If every one had the machine to which Dr. Bloodgood referred, with a 200 kilowatt power, and if there was a standardized dosage and technic, it might possibly be safe to attempt treatment along this line; but it is evident that the treatment that may be safe in the hands of well equipped, well trained personnel conceivably is not a safe thing to be adopted by the general profession. In my earlier experience I endeavored to preserve the breasts of these patients with so-called borderline tumors. One of them came back within eight months with recurrent growth in the breast, and two others came back still later with recurrences in the breast and axillary node metastasis. After that I came to the conclusion that a tumor is either benign or malignant, and if the pathologist could not assure me of the malignancy of a given growth and wasn't positive as to its nonmalignant nature, the patient would be safer with a simple or a conservative mastectomy in order to prevent local extension and recurrence.

DR. MAX CUTLER, Chicago: Dr. Bloodgood raised several important questions on radiation therapy of mammary cancer. Difference of opinion exists on this subject, which because of inadequate data is at present a subject of controversy, even among those who have had the greatest experience with this problem. I should like to make the following observation: Three major difficulties are encountered in the radiation treatment of mammary cancer: 1. The extensive surface area that must be regarded as potentially involved, regardless of how early the lesion appears to be on clinical examination. 2. The relative radioresistance of most malignant tumors of the breast. 3. The difficulty and uncertainty of effective irradiation of the axillary lymphatic glands. According to the latest conceptions of dosage and technic, the amount of radiation that is necessary to sterilize the more radioresistant forms of mammary cancer is such as to preclude the subsequent radical surgical removal of the breast with safety. Thus the present development of radiation leads to a more effective treatment of mammary cancer when radiation alone is used rather than when radiation is combined with surgery. The use of preoperative radiation in moderate doses can be defended on the basis that there exists a small group of carcinomas of the breast that is moderately radiosensitive. Clinical and pathologic evidence is available to demonstrate that this small group can be sterilized by a dose of radiation that can be followed safely by the radical surgical operation. I utilize preoperative radiation under two circumstances: 1. In lesions of clinical borderline operability. 2. In lesions in which the clinical setting and microscopic evidence, when available, indicate the presence of a highly malignant anaplastic carcinoma, particularly in younger women. Most statistical evidence attempting to prove the value, or lack of value, of prophylactic postoperative irradiation is contradictory, subject to numerous fallacies, and insusceptible of withstanding critical analysis. When the complete radical operation is performed on an early localized carcinoma of the breast and the axillary lymphatic glands are not invaded, it is difficult to defend the routine use of prophylactic postoperative irradiation, although this procedure has been generally adopted by most clinics. Since postoperative irradiation can be administered with complete safety and its use entails no risks or delays, most radiologists advise this procedure as a precaution. When microscopic examination of the tumor indicates a highly anaplastic carcinoma or when the axillary lymphatic glands have been invaded, there is considerable evidence to indicate prophylactic postoperative irradiation, and I utilize it under these circumstances. Because of the fact that when irradiation precedes surgery the dose of radiation must be reduced, it is entirely inadequate to control the more radioresistant forms of mammary cancer. Because of this fact the restriction of the extent of the surgical procedure is entirely unsound and dangerous. Under no circumstances should the extent of the radical operation for mammary cancer be reduced, either because the lesion is small or because irradiation is combined with the surgical procedure.

DR. J. C. BLOODGOOD, Baltimore: I thank Dr. Abell and Dr. Cutler. I am sorry they didn't read to you the letter I wrote them in which I said that if they could possibly differ with me I wished they would. I was trying to bring the borderline tumors before the profession. At least I have no evidence that, if there is a little delay between the removal of this clinically benign tumor and the radical operation, if it is proved to be malignant, delay is dangerous. I cannot give the evidence in the time allotted here, but I have evidence to prove the statements I have made. Therefore the pathologists throughout this country must be given an opportunity to prepare themselves to recognize the borderline tumors that are malignant. Not every hospital can be furnished with such a trained pathologist. Therefore the operators, when their own pathologists are unable to diagnose the breast tumor, must send it to two or more of these diagnostic clinics for their view, and when two or more such diagnostic clinics differ the operator may conclude that the tumor is benign. During this period when sections of the borderline breast tumor are submitted to other pathologists the axilla of the patient can be treated with high voltage roentgen therapy, and if there is further delay after ten days the breast can be irradiated. If the positive diagnosis of malignancy comes in then, radiation treatment can be stopped and after an interval of one week or ten days the complete operation for cancer performed.

The Fertile Period in Monkeys.—The female monkey, which is the only animal to show a true and regular menstrual bleeding, has a menstrual cycle lasting on the average from twenty-seven to thirty days (Corner, E. Allen, Hartman, Joachimovits, Spiegel and Zuckerman). In contrast with other animals, which have a distinct heat and, as a rule, only copulate during this time, the female monkey allows access to the male at all parts of the menstrual cycle, but she does not become pregnant after every coitus. This animal, therefore, also manifests a periodic alternation of fertility and sterility. Hartman, who carried out a lengthy series of experiments on a large and well supervised colony of monkeys to determine the boundary between the fertile and the sterile periods, found that out of 420 acts of intercourse, which took place on all days of the menstrual cycle, only 52 led to pregnancy, and that out of these 52 conceptions, 49 took place between the eleventh and sixteenth days inclusive. Hartman found a fertility rate of 25 per cent on the eleventh day, 11 per cent on the twelfth and thirteenth days, and 25 per cent on the fourteenth day. There is, in fact, such a sharp line between the sterile and fertile days of the monkey that Hartman is perfectly justified in saying that these animals have a "safe period."—Knaus, Hermann: Periodic Fertility and Sterility in Woman, Vienna, Wilhelm Maudrich, 1934.

THERAPEUTICS OF THE INTRAVENOUS DRIP

FURTHER OBSERVATIONS

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In a previous report [1] dealing with the influence of velocity on the response to intravenous injection, the physiologic advantages of the slow intravenous drip were stated. Later,[2] a convenient apparatus for the clinical use of the drip was described together with details for preparing sets and solutions.[3] In analyzing 100 consecutive requests for these sets, the therapeutic indications [4] included the treatment of (*a*) hemorrhage, (*b*) shock, (*c*) the infectious medical and surgical diseases, (*d*) the prevention of complications in extensive or shock-producing surgical procedures, (*e*) the prophylaxis and treatment of thyrotoxic crises, (*f*) the

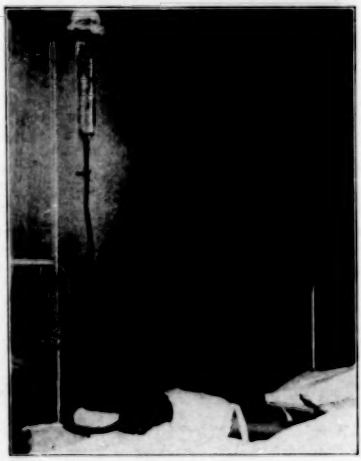

Fig. 1.—Complete assemblage of intravenous drip, showing the set in use with the arm of the patient strapped to a fracture board.

alleviation of postoperative complications such as ileus, gastric dilatation, vomiting and anuria, (*g*) the treatment of various metabolic and toxic conditions, such as the alimentary toxicosis of infancy,[5] dehydration resulting from uncontrollable vomiting or intractable diarrhea, urinary suppression and diabetic ketosis, and (*h*) the treatment of exogenous poisoning. In the thirty months since January 1932, 9,471 sets have been employed in the hospital—an average of ten sets daily. The frequency with which the sets have been used is sufficient proof of the widespread adoption of this method and its great utility.

The present communication deals further with the therapeutics of the intravenous drip as illustrated by a series of 1,000 consecutive experiences.

AS A PROPHYLACTIC AND SUPPORTIVE IN VARIOUS SURGICAL CONDITIONS

There has been an increasing tendency on the part of surgeons to use the drip as a supportive during the critical period of the operative manipulation, or as a prophylactic against complications. Drips for these purposes were started before the patient came to the operating room, during the course of the operation, or immediately after the patient was returned to the ward.

A. *In Appendicitis with Peritoneal Complications.*—Sixty-six patients who were admitted to the hospital with acute appendicitis complicated by peritonitis or local abscess formation were given prophylactic intravenous drips. The clinical course was often complicated further by intestinal obstruction, multiple intraperitoneal abscesses, subphrenic collections of pus, or sepsis. Many of these patients were admitted with moderate or marked temperature elevation and occasionally with chills. Despite this, Dr. Harold Neuhof, a pioneer in intravenous therapy,[6] had no hesitancy in employing the drip. In instances in which postoperative chills or elevation of temperature occurred, a search for complications was carefully instituted before the culpability of the drip was considered. With the onset of complications or spread of infection, the patient's welfare necessitated the continuance of the drip as a therapeutic endeavor. This was often rewarded by recovery in the presence of grave prognostic signs.

B. *In Surgery of the Gastro-Intestinal Tract.*—The prophylactic intravenous drip has also been extensively used by Dr. A. A. Berg [7] in formidable procedures on the gastro-intestinal tract. Two hundred and eighteen patients were included in this group. One hundred and thirty-six were subjected to resection of the stomach, duodenum or jejunum. Thirty-four patients had cancer of the stomach, and forty-three had peptic ulcers. In sixteen, perforation or penetration of the bowel had occurred and eight had secondary resections for gastrojejunal ulcers. Four of the group had had massive hemorrhages; there were eight with pyloric obstruction and two with pancreatic abscess, as the result of penetration or perforation of peptic ulcers. One patient had a complicating cirrhosis of the liver, another a mitral stenosis, and a third diabetes mellitus. In the majority of instances Dr. Berg was able to accomplish resection of the bowel and anastomosis.

Eighty-two patients had lesions involving the lower part of the bowel and of these seventy had carcinoma of the colon, sigmoid, cecum or rectum. Seven patients had intestinal obstruction from various causes, and the rest had miscellaneous conditions such as stab wounds, regional ileitis, diverticulitis, ulcerative colitis, intussusception, perforation by foreign bodies or volvulus.

In the majority of the patients with carcinoma of the large bowel, Dr. Berg successfully performed resection

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Read before the Section on Pharmacology and Therapeutics at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 15, 1934.

1. Hirshfeld, Samuel; Hyman, H. T., and Wanger, Justine J.: Influence of Velocity on the Response to Intravenous Injections, Arch. Int. Med. **47**: 259 (Feb.) 1931.
2. Hyman, H. T., and Hirshfeld, Samuel: Studies of Velocity and the Response to Intravenous Injections: Technic of the Intravenous Drip, J. A. M. A. **96**: 1221 (April 11) 1931.
3. Lewisohn, Richard, and Rosenthal, Nathan: Prevention of Chills Following Transfusion of Citrated Blood, J. A. M. A. **100**: 466 (Feb. 18) 1933.
4. Hyman, H. T., and Hirshfeld, Samuel: The Therapeutics of the Intravenous Drip, J. A. M. A. **100**: 305 (Feb. 4) 1933.
5. Karelitz, Samuel, and Schick, Béla: The Treatment of Alimentary Toxicosis, J. A. M. A. **99**: 366 (July 30) 1932.
6. Neuhof, Harold, and Hirshfeld, Samuel: Administration of Sodium Citrate to Control Bleeding, Ann. Surg. **76**: 1 (July) 1922.
7. Berg, A. A.: Mortality and Late Results of Subtotal Gastrectomy for Radical Cure of Gastric and Duodenal Ulcer, Ann. Surg. **92**: 340 (Sept.) 1930.

and anastomosis. The drip was employed by him in several ways. In the less complicated cases it was started during or just after the operative procedure to tide the patient over the first few postoperative hours or days and to maintain nutrition, so that oral feeding might be minimized. In patients who were malnourished or anemic, the drip was used preoperatively to build up the general resistance and to correct the anemia

Fig. 2.—The metal case container devised by Dr. Joseph Turner and provided with slots to permit the entrance of steam during autoclaving.

by the introduction of citrated or whole blood. This type of preparation enabled Dr. Berg to execute major procedures in many patients who, on admission, seemed impossible surgical risks, and helped to support others beyond the critical period.

C. *In the Surgery of the Chest and Nervous System.*—In similar fashion, Drs. Harold Neuhof and Ira Cohen, respectively in charge of surgery of the chest and the nervous system, employed the intravenous prophylactic drip as a routine in all serious exigencies that arose in these special fields. In the thoracic service it was almost an invariable custom to start the drip in the operating room in thoracoplasty, pneumotomy, lobectomy, or extensive rib resection in adults, and with simpler suppurative lesions of the pleurae and lungs in infants and young children.

In the surgery of the brain and spinal cord, hypertonic dextrose solutions were of added value in decreasing intracranial tension.[8]

D. *In Surgery of the Biliary Passages.*—There seemed to be an increasing tendency to employ the drip in procedures involving the liver and biliary passages. The coexistent disturbances in carbohydrate metabolism, the tendency to bleed, especially in the presence of jaundice, and the metabolic hyperpyrexia that is not uncommonly seen following surgical manipulation in this field furnished ideal indications for the use of a prophylactic drip. In secondary procedures on the biliary passages, the drip was employed prophylactically in virtually every instance.

E. *In Genito-Urinary Surgery.*—In genito-urinary surgery, Dr. Beer and his colleagues used the drip prophylactically most commonly, in an attempt to maintain adequate urinary secretion. Reflex oliguria and anuria with resultant azotemia are frequent and serious complications following manipulation of the genito-urinary passages. These were experienced particularly in elderly patients whose kidneys had been damaged by prolonged urinary retention or infection. Intravenous dextrose exerted a beneficial diuretic action.

F. *In Thyroid Surgery.*—In surgery of the thyroid gland Dr. Lewisohn used the prophylactic drip in the severe or complicated cases of exophthalmic goiter. It has been our practice [8a] however, to use the drip as a routine in all operations on the thyroid gland, because of the uncertainty of predicting the occurrence of thyrotoxic storms.

G. *In the Surgery of Diabetes.*—In surgery on diabetic patients, the management of the metabolic condition was greatly facilitated by the use of the prophylactic drip. The risk in operating on these patients was usually out of all proportion to the actual extent of the surgical procedure. Simple postoperative complications, particularly vomiting, may readily produce a ketosis. A valuable method of preventing unfortunate sequelae was the liberal supply of fluid, dextrose, saline solution and insulin by the prophylactic intravenous drip.

H. *In Surgery of Hemorrhagic Diseases.*—Patients who had hemorrhagic diatheses, from whatever cause, and who were subjected to surgical procedures were given the advantage of the drip. The introduction of citrated or unmodified blood not only replaced the lost blood but also aided in increasing coagulability. Dr. Nathan Rosenthal, who is in charge of the hematologic cases, constantly made use of the drip for these purposes.

USE OF THE INTRAVENOUS DRIP FOR COMPLICATIONS THAT OCCUR FOLLOWING SURGICAL PROCEDURES

In a previous paper [4] the therapeutics of the drip in the actual treatment of surgical complications was amply described and needs little elaboration. In the management of hemorrhage, shock, postoperative vomiting, gastric dilatation, ileus, anuria, oliguria and sepsis, indications were clearly defined and the drip was of incalculable value.

Fig. 3.—The contents of the metal container, showing the gravity flask, the short piece of rubber tubing with the glass drip and a clamp, a long piece of rubber tubing with the stopcock and the long glass connection, and a short piece of rubber tubing with the adapter for the needle.

When these symptoms arose, the drip was also employed advantageously for the introduction of drugs and biologicals. In shock or collapse, the value of the drip was enhanced by ephedrine or epinephrine. In postoperative ileus, the introduction of ampoules of pitressin into the rubber tubing above the needle was effectively carried out. Acidosis following vomiting, in diabetic and nondiabetic patients, was treated by the introduction of alkali or dextrose together with adequate amounts of insulin. In sepsis, whole blood was used nonspecifically and, if a specific antibody was available, the serum was dripped in constantly so that enormous dosages were introduced with little risk or reaction. In the thyrotoxic storms of exophthalmic goiter, iodides were added directly. In two instances of acidosis resulting from the use of massive doses of ammonium chloride or sodium phosphate, sodium

8. Kennedy, Foster, and Wortis, S. B.: Modern Treatment of Increased Intracranial Pressure, J. A. M. A. **96**: 1284 (April 18) 1931.
8a. Hyman, H. T., and Kessel, Leo: Studies of Exophthalmic Goiter and the Involuntary Nervous System: Treatment of Patients with Disturbances of the Thyroid Gland, J. A. M. A. **96**: 2014 (June 13) 1931.

bicarbonate administered intravenously promptly corrected the metabolic disorder.

In traumatotherapy the drip found a great sphere of usefulness in combating both shock and hemorrhage. In skull injuries, the intravenous introduction of hypertonic solutions accompanied by repeated lumbar taps aided in the adjustment of pressure relationship within the cranial cavity.[8]

Fig. 4.—A close view of the method of maintaining the needle in the vein by means of sterile adhesive tape.

In extensive burns, drips of dextrose with saline and blood were of the greatest value in correcting dehydration and in combating anuria.

THE USE OF THE INTRAVENOUS DRIP IN INTERNAL MEDICINE

Many of the uses of the drip in internal medicine have already been indicated in the discussion of the surgical procedures. In the management of ketosis in diabetes, in the treatment of azotemia in nephritis, in the dehydration that occurs with toxic vomiting or intractable diarrhea in infants [8] or adults, in hemorrhage and in the hemorrhagic diatheses, the indications and procedures were self evident. In poisonings with carbon monoxide, barbiturates, morphine, mushrooms, arsenic, colocynth, corrosive mercuric chloride, and the cholemia that resulted from cinchophen poisoning, the drip was often of great value. In one instance of bromism with cerebral symptoms, the chloride in the drip was utilized to replace the bromide ion.

There is great promise in the extension of the use of the drip in the introduction of massive doses of specific serums and drugs. With specific serums, for example, it was a comparatively simple matter to introduce daily from 200,000 to 300,000 units of pneumococcus, tetanus or diphtheria antibody in the course of a continuous drip. Serum reactions were greatly minimized by the slow introduction of diluted agents.

With Chargin and Leifer,[9] we have conducted experiments in massive chemotherapy. Twenty-five male patients with primary seropositive or secondary syphilis received an average of 4 Gm. of neoarsphenamine in a period averaging five days. No serious or permanent early or late parenchymal changes occurred in these patients, though febrile reactions were common and at times alarming. Wassermann negativity was obtained in 95 per cent of the nineteen cases followed beyond the critical period of three months, though neither bismuth nor mercury compounds were employed. This work is still in the experimental stage. It is extremely suggestive and may prove of great value.

9. Chargin, L.; Leifer, W., and Hyman, H. T.: The Application of the Intravenous Drip Method of Chemotherapy as Illustrated by Massive Doses of Neoarsphenamine in the Treatment of Early Syphilis, to be published.

UNTOWARD REACTIONS OF THE DRIP

Drips were frequently maintained for several days, and in one instance a drip ran for three weeks. Many patients had intermittent drips, so that the total number of sets used far exceeded the number of patients. Despite this, difficulties arose on only thirty-eight occasions, usually because of chills or febrile reactions.

A. *Chills During Transfusion.* — Chills followed transfusion eleven times: eight by the citrate and three by the direct method. Citrate transfusions were used proportionately more frequently than direct transfusions. Once a chill occurred with citrate transfusion and then the direct method was employed without chill. Contrariwise, in one instance in which the direct method was followed by a chill, the citrate method was used without reaction. The citrate method, introduced by Dr. Richard Lewisohn [10] at our hospital in 1915, is so simple that we find no valid reason for recommending the more complicated direct method. The citrate transfusion was often performed without the patient's knowledge and did not require the complicated set-up or the technical skill necessary with the direct methods. To our knowledge, the direct method possessed no positive advantages, and reactions were no less frequent.

B. *Chills Resulting from the Underlying Pathologic Process.*—In fifteen instances, chills occurred during the course of a drip but seemed the result of the underlying pathologic condition. In six cases each of extensive genito-urinary infection, or peritoneal involvement, rigors occurred. Often the drip had run for many hours before or after the chill. In one instance each the hyperpyrexia probably was caused by thyrotoxicosis in exophthalmic goiter,[11] the terminal febrile elevation of diabetic coma,[12] or the onset of pneumonia.

C. *Chills Resulting from Technical Errors in the Preparation or Administration of the Drip.*—There remained twelve instances of chills resulting from the drip. In eight of the twelve, the chill occurred at the onset of the drip, probably owing to contamination of

Fig. 5.—The same as in figure 4 with most of the adhesive tape removed.

the solution by some pyrogenic substance.[13] In four other instances the chill occurred during the course of the drip. These reactions ceased when analytic reagent sodium chloride, packed in individual stoppered bottles, was substituted for chemically pure sodium chloride, distributed in small barrels, and when a carboy

10. Lewisohn, Richard: New and Greatly Simplified Method of Blood Transfusion, M. Rec. **87**: 127 (Jan. 23) 1915.
11. Kessel, Leo, and Hyman, H. T.: Exophthalmic Goiter (Graves' Syndrome) and the Involuntary Nervous System: XI. Causes of Death, J. A. M. A. **84**: 1720 (June 6) 1925.
12. Lande, Herman: The Uncontrollable Causes of Death in Diabetic Coma, J. A. M. A. **101**: 9 (July 1) 1933.
13. Banks, H. M.: Hyperpyrexic Reaction Following Intravenous Therapy, Am. J. Clin. Path. **4**: 260 (May) 1934.

used as a reservoir for the triple distilled water was thoroughly cleansed. In each instance it was thought that pyrogens had been introduced by these apparently trivial lapses in vigilance. We are in complete agreement with our colleagues Drs. Lewisohn and Rosenthal,[3] who state, in speaking of the reactions following citrate transfusion, that these occurrences are preventable and invariably due to some technical error. Safety is obtained only by eternal vigilance and in our institution we are particularly indebted to Miss Anna Koch, who is in charge of the central room for the preparation of intravenous sets, and to Dr. Nathan Rosenthal, who supervises this department. Even with technically perfect sets, however, reactions will occur unless the clinician is equally careful in performing his end of the set-up of the drip, and the current craze for speed will be penalized by reactions, particularly when the vehicle contains pyrogenic substances.

DEATHS ASSOCIATED WITH DRIP THERAPY

More important than the febrile reactions and chills, which in themselves did not seriously or permanently jeopardize the patient's chances for recovery, were two instances in which death occurred:

CASE 1.—A woman with exophthalmic goiter, who was admitted during a severe thyroid storm, received the drip on two successive days, following which she was given 125 cc. of citrated blood. The drip had been administered with impunity, but following the citrated blood she had a chill lasting forty minutes, her temperature rose to 108 F., and she died within twenty-four hours.

CASE 2.—A man with a cancer of the rectum, who had had a resection of the bowel and a permanent colostomy, was given a postoperative prophylactic drip for four days; he did well for two weeks, and then a severe diarrhea developed and the patient became dehydrated. The drip was resumed and was followed by a severe chill and a rise in temperature to 108 F. Death occurred four hours later. Autopsy showed no cause of death.

The history in each of these instances strongly indicates that the drip might have contributed to the fatal termination. While terminal hyperpyrexia occurs as part of the clinical syndrome in thyroid "storms,"[11] no such explanation can be afforded in the carcinoma fatality.

MISCELLANEOUS NOTES

Though many of our patients were desperately sick and often moribund, at no time did we encounter any circulatory complications that might have resulted from the introduction of the fluid. Local pain and discomfort were frequent complaints and usually responded to changes in position or to sedatives or narcotics. There were no significant local inflammatory processes in the skin or the veins.

As the drip requires frequent adjustment, the patients must be seen from time to time to regulate the rate of flow, add solution or change the position of the arm. This frequently imposed an extra burden on the nursing facilities, particularly when the ward services were active. Under these circumstances, if special nursing was not possible, the drip was removed during the night hours and resumed during the daytime, when more members of the staff were in active attendance.

Physicians who practice in outlying communities and who lack hospital facilities for the sterilization of apparatus and solution may take advantage of the ingenious sets that have been commercially devised and that can be purchased and stored indefinitely.[14] These sets are easily assembled and are free from pyrogenic substances. In our limited experience these sets have been completely satisfactory.

For the benefit of the many clinicians who harbor the fear that an intravenous drip might tend to elevate blood pressure and thus cause or perpetuate bleeding, it is important to note that no such occurrence was encountered in the entire series.

During the course of prolonged intravenous infusions, the patients should frequently be examined for peripheral edema or edema of the lung. At times these may be due to excessive amounts of salt, under which circumstances distilled water may be substituted with from 5 to 50 per cent dextrose. If the edema is severe, the drip must be discontinued temporarily and the patient placed on limitation of fluids or mercurial diuretics.

ABSTRACTS OF CASES ILLUSTRATING THE VALUE OF THE DRIP

The value of the drip may be emphasized by citing briefly illustrations of its use in specific instances in which immediate recovery occurred:

CASE 3.—In a patient with tonsillitis, an acute glomerulonephritis and uremic coma, the drip ran for three days, following which the patient had clyses for four days. Four weeks later the patient had a tonsillectomy without any difficulty.

CASE 4.—A patient had a subacute yellow atrophy following the use of cinchophen derivatives. She was admitted with jaundice and fever. The drip ran for two days until the acute symptoms disappeared.

CASE 5.—In a patient with a carcinoma of the sigmoid, a colostomy was attempted under spinal anesthesia and shock ensued. The drip was started in the operating room, ephedrine and epinephrine were added to the fluid, and artificial respiration was instituted for the respiratory paralysis. The operation was completed, the drip continued to run for two days, and the patient made a complete recovery.

CASE 6.—A diabetic patient had a duodenal ulcer with pyloric obstruction. Vomiting was persistent and acidosis developed. A drip of dextrose with insulin was given and at the end of three days the patient was in excellent condition. Shortly thereafter the patient was readmitted with hematemeses from the ulcer. Three transfusions of citrated blood were administered, a gastro-enterostomy was performed, and a postoperative prophylactic drip was used for two days.

CASE 7.—A child, aged 4 years, suffered extensive first and second degree burns of the face, chest and abdomen, with marked toxemia. A drip was instituted for two days and citrated blood with dextrose was introduced, with gratifying results.

CASE 8.—A pregnant woman was admitted with the symptoms and signs of an acute surgical condition of the abdomen, shock and persistent vomiting. Because the indications were not clear, the surgeons wisely decided to temporize, and the drip was instituted for twenty-four hours. Following this the symptoms abated, and the patient recovered and was discharged.

CASE 9.—In this case definite indications for operative intervention abated after the use of the drip for a few days. The patient had a pyloric obstruction from a duodenal ulcer and was admitted with persistent vomiting. He refused operation and was placed on a drip for three days, after which the vomiting subsided and the obstruction disappeared.

CASE 10.—A man with a pyelonephritis was admitted in uremia with a urea nitrogen of 108 mg. per hundred cubic centimeters of blood. The drip was continued for three days; the urea nitrogen fell to 46 mg. per hundred cubic centimeters and the patient recovered sufficiently to be discharged from the hospital.

CASE 11.—A patient had a combination of pernicious anemia, diabetes mellitus and cirrhosis of the liver. He was admitted in coma that was probably the result of a combination of hepatic insufficiency and ketosis. The blood sugar was 300 mg. A drip ran for two days and the patient recovered from the acute episode.

14. The Titus intravenous infusion apparatus (J. A. M. A. **100**: 1104 [April 8] 1933) and the sterile dextrose in physiologic solution of sodium chloride in vacoliter containers prepared by the Don Baxter Intravenous Products Corporation (J. A. M. A. **102**: 1154 [April 7] 1934).

Case 12.—A patient injured in a traffic accident had a contusion of the lung with a pleural effusion and marked shock. The drip was instituted for two days and recovery followed.

Case 13.—A patient presented a complicated clinical picture of diabetes mellitus, hypertension and a twisted ovarian cyst. A drip of dextrose and insulin was started before operation and was followed in an hour by a chill and a temperature of 102 F. The drip was discontinued but after operation was resumed again, and the patient made a complete recovery. Shortly thereafter she was readmitted with an incarcerated umbilical hernia and intestinal obstruction. Vomiting was persistent. A drip of dextrose and insulin was again instituted and was continued through the hernioplasty and for two days later, after which convalescence was uneventful.

Case 14.—A man with a tabetic bladder and prostatic hypertrophy was admitted in uremia. The drip ran for four days and the patient's condition was sufficiently improved so that the presacral nerves could be resected and a suprapubic cystostomy performed, after which a normal convalescence occurred.

Case 15.—A patient entered the hospital with a toxic hepatitis and gastro-enteritis from arsenical intoxication and a syphilitic iritis. A drip of 10 per cent dextrose with insulin was administered for four days and recovery followed.

Case 16.—This illustrates one of the several instances in which, following acute appendicitis with peritonitis, postoperative ileus developed. A drip was started, the stomach drained by a Levin tube and the ileus controlled, and later an intraperitoneal abscess ruptured spontaneously through the wound.

Case 17.—This is also illustrative of several instances in which an incarcerated hernia caused vomiting and distention. The drip was started, the hernia was manually reduced, the bowels again functioned and, after a free period of a week, a hernioplasty was performed.

Case 18.—This was one of several instances of emergency surgery in diabetes. An acute cholecystitis with cholelithiasis developed in a patient. The blood sugar was 270 mg. per hundred cubic centimeters and acetonuria was marked. A drip of dextrose and insulin was started; a cholecystostomy and drainage was performed; the drip was continued for four days, after which the patient recovered and the diabetes was easily controlled.

Case 19.—Another surgical diabetic patient was admitted in diabetic coma and with a carbuncle of the lip. The blood sugar was 400 mg. per hundred cubic centimeters; the carbon dioxide combining power was 11.5 volumes per cent, and acetonuria was marked. A drip of dextrose and insulin ran for two days. The blood sugar fell to 60 mg.; the carbon dioxide combining power rose to 57 volumes per cent; the carbuncle of the lip responded to conservative treatment, and the patient was discharged.

Case 20.—This case illustrates the control of the vicissitudes that occur in elderly patients with prostatic hypertrophy. This patient had a first-stage prostatectomy followed by profuse hemorrhage. A drip was given with epinephrine and caffeine, and citrated blood was later introduced. The drip ran for four days, following which the second stage was done with an uneventful convalescence and recovery.

Case 21.—This illustrates another use of the drip in the treatment of poisoning. The patient had barbiturate intoxication and remained in coma for two days, after which the drip was started. In sixteen hours the patient regained consciousness and made a complete recovery.

Case 22.—This is one of several instances in which azotemia occurred during the course of operative intervention on the biliary passages. The patient had a cholecystectomy, and a postoperative prophylactic drip was run for a day and a half. After the cessation of the drip, the blood urea nitrogen rose to 66 mg. per hundred cubic centimeters and the temperature to 103 F. On the sixth day the patient was stuporous and the drip was resumed for four days, during which time the temperature and urea nitrogen fell to normal.

Case 23.—This illustrates an unusual instance of acidosis, probably from the excessive use of ammonium chloride. Following a suprapubic prostatectomy for fibro-adenoma of the prostate, the patient's blood pressure fell from 160 to 100, he became stuporous and signs of acidosis developed, with 14 volumes per cent of carbon dioxide combining power of the blood. A drip was run for twelve hours, beginning with sodium bicarbonate. The patient reacted thirty minutes after the institution of the drip and made a recovery.

Case 24.—A patient in whom the persistent use of the drip was rewarded by an extraordinary recovery had a common duct stone with jaundice, and a cholecystectomy and choledochotomy were performed. A postoperative prophylactic drip ran for three days. On the fifth day the patient went into collapse from an intraperitoneal hemorrhage, which later became infected. For the next three days the drip was used and citrated blood was added on two occasions. After an intermission of four days this therapy was again resumed for fifteen days. On the twelfth day a direct transfusion was performed, and a chill ensued. The transfusion was repeated without a chill and the patient went on to make a complete recovery.

Case 25.—The use of the drip in preparing patients for operation is well illustrated in a patient who had a bleeding and penetrating duodenal ulcer. For nineteen days the patient was given daily drips and two citrate transfusions. A subtotal gastrectomy was then performed and a postoperative prophylactic drip was started and fortified with a pint of citrated blood. The drip ran for four days, during which time another pint of blood was introduced, and the patient recovered.

Case 26.—This is one of several complicated renal cases in which bilateral calculi occurred. A right nephrostomy and left ureterolithotomy were performed. The blood urea nitrogen rose on the first postoperative day to 53 mg. per hundred cubic centimeters. A drip was run for two and a half days and the patient was markedly improved. On the thirteenth postoperative day a pain in the left side and anuria developed. The drip was resumed for four days. Four months later a right nephrectomy was done, following which postoperative vomiting occurred. After a drip that ran for a day and a half, the symptoms were alleviated.

SUMMARY

The intravenous drip has won a permanent place in therapy in our institution. The use of 9,471 sets in thirty months, or of ten sets daily, gives numerical testimony on this point. These figures are supported further by a comparison of the number of intravenous and hypodermoclysis sets that have been used in this period. In 1932, 3,235 intravenous sets were ordered, and 2,157 clysis sets; in 1933, 4,287 of the intravenous sets were used, and but 1,539 subcutaneous sets. To date in 1934, 1,949 intravenous sets have been used, and only 322 clysis outfits. In comparsion with hypodermoclysis, the intravenous drip has the advantage of more certain absorption, greater adaptability, less discomfort to the patient, and the possibility of adding drugs and whole blood directly into the circulation. At the seemingly slow rate of 2 or 3 cc. per minute, the drip will introduce daily between 2,500 and 4,000 cc. of fluid and may be continued for several days or even weeks, as in patient 18, who received a drip for twenty-four days.

Once the drip is in operation, it is impressive to observe the ease of management of extremely difficult and complicated conditions. By the single technical procedure the problem of nutrition and of the introduction of fluid, salts, drugs, blood and serum becomes automatic.

940 Park Avenue.

ABSTRACT OF DISCUSSION

Dr. T. G. Orr, Kansas City, Mo.: This important means of therapy is growing in popularity. Continuous venoclysis has been emphasized very much in recent years. The work of Hyman and Hirschfeld has been especially important in introducing the term "speed shock," perhaps not of the term itself, but of emphasizing the importance of speed in giving intravenous solutions. They have shown conclusively that many solutions can be given safely if they are given slowly enough. There are four major dangers, perhaps not so great if given properly, but nevertheless constantly present: (1) the immediate

reaction; (2) the possibility of overloading the circulatory tree; (3) the production of edema; (4) the production of pulmonary embolism. Any one of those four, I believe, may happen, although perhaps not very frequently. Two or three deaths that occurred recently may have been caused by pulmonary embolism, secondary to continuous venoclysis. This led to experimental work, which has been carried out in the University of Kansas surgical clinic by Dr. Mervin Rumold in animals, continuous venoclysis being given as long as the animal lived. He has done this work in several series of experiments with simple salt solution, dextrose in 10 per cent solution, a combination of the two, and by simply placing cannulas and needles in the vein. In every instance he found pulmonary involvement after experimental introduction of these solutions. There is a local irritation of the vein, in which a thrombus forms. Emboli break off and float into the lung. Experimentally, there is certainly definite danger in giving continuous venoclysis by the drip method. Solutions were given very slowly, the animals watched twenty-four hours of the day, and inspected every hour to see that the solutions were running properly. In every single instance there were pulmonary complications. It is to be remembered that nature never intended feeding, watering and treatment to be given by vein and that the insult should be properly respected.

DR. PAUL TITUS, Pittsburgh: The indications presented for prolonged, slow intravenous medication seem to be many, but probably they are still incomplete. The advisability of terming this "intravenous drip" is questionable, however, and I prefer Hendon's term, prolonged "venoclysis," or that of Fantus, "phleboclysis." The solution does not drip into the vein; it runs in a steady, slow stream through the needle, even though a glass drip bulb is sometimes used to measure the rate of flow. Other instruments, such as the one devised in our clinic for several different types of intravenous injections of dextrose, have a valve instead of the drip bulb for this slow flow, and the term "drip" may give an incorrect impression of the operation. Being convinced of the therapeutic value of the prolonged venoclysis, I should have liked to hear more about flow rates and total dosages. My colleagues and I have been interested in the intravenous use of dextrose solutions in pregnancy toxemia and gynecologic surgery. Clinicians are not dependent on prolonged venoclysis for this, as prolonged injection is not always necessary; but we have available single large therapeutic doses of dextrose (from 75 to 100 Gm.) that may be given faster than the prolonged venoclysis. For example, a 25 per cent solution should be given at 3 cc. per minute in an average sized adult to maintain the physiologic rate of Wilder and Samson; namely, 0.8 Gm. per kilogram of body weight per hour, and weaker solutions proportionately faster. The proper rate may easily be computed. Venoclysis of dextrose solution, if prolonged for hours or days in a patient who particularly needs this on account of various chronic states or dehydration, must be given much more slowly than single doses in order to avoid pancreatic stimulation and overproduction of endogenous insulin with hypoglycemic reactions and shock in the actual presence of an intravenous injection of dextrose, if such a parodoxical fact can be accepted. On this account the concentration of the dextrose solution must be reduced for venoclysis to 5, or at the most 10 per cent, while the flow rate must also be slowed down, like that of the hypertonic solutions, to not more than 4 or 5 cc. per minute, in order to avoid this overstimulation of the pancreas, whereupon venoclysis may be prolonged indefinitely to the great benefit of the patient.

DR. ROBERT KAPSINOW, Lafayette, La.: The intravenous drip is indicated in every condition that results in a blood concentration. This includes the entire field of anhydremia. The mechanism of anhydremia may be divided into three groups: those due to simple water deprivation, those due to excessive fluid lost either through profuse vomiting, sweating or diarrhea, and, lastly, those conditions produced by a loss of fluid from the blood stream due to increased capillary permeability. In the first group, including such conditions as water deprivation on the desert for example, or as found in the mentally deranged, patients are quickly restored by the administration of relatively small amounts of fluid introduced through any channel. In the second group are cases of profuse sweating in deep mines or in boiler rooms. Large volumes of fluid containing sodium and chlorine ions are lost in the profuse vomiting of pregnancy, high intestinal obstruction in adults and pyloric obstruction in infants. Numerous drugs likewise incite pernicious vomiting. Various gastric and intestinal fistulas rapidly lead to depletion of the water storage of the body. The severe diarrheas of cholera or the bacillary types of dysentery, colitis of the ulcerative or tuberculous type, the diarrheas of infancy or the excessive use of purgatives may account for the loss of many liters of fluid daily. This group requires more than the simple administration of plain water. Either sodium chloride or dextrose must be administered. In this group, any method of introduction of fluids will avail. In the third group, resulting in anhydremia due to loss of fluid from increased capillary permeability, the intravenous drip is the most important. These are gas poisoning, influenza, extensive superficial burns, eclampsia, severe urticarial phenomena, acute medical shock or histamine or peptone shock.

DR. HAROLD T. HYMAN, New York: Dr. Titus's criticism of our title is just. We use the term "intravenous drip" or "slow intravenous drip" in order to emphasize to the clinicians the necessity of doing this procedure slowly. In our own institution, and despite everything we may say, we find, in a crisis, that the interns become alarmed and turn the drip on as rapidly as possible. Concerning Dr. Orr's warning about reactions, I wish to emphasize that. I think that it is only fair, though, to point out that one cannot compare conditions in a rabbit weighing 4 or 5 Kg. and those in a normal individual weighing 50 or 60 Kg. One cannot give a continuous slow intravenous drip in a rabbit at a rate comparable to 2 cc. a minute without that drip stopping up. If it does run, it means that the rabbit is getting comparatively more fluid, and under those circumstances there will be edema of the lungs and emboli. In our clinical experience, even in two fatal cases, we did not find pulmonary emboli. If pulmonary emboli occur, it is probably due to a technical error comparable to what we call speed shock.

THE METABOLISM OF LEVULOSE

VI. THE INFLUENCE OF THE LEVEL OF OVARIAN FUNCTION

ALLAN WINTER ROWE, PH.D.
MARY A. McMANUS, A.B.
AND
ALBERT J. PLUMMER, A.M.
BOSTON

Earlier communications on the levulose tolerance have dealt severally with certain general conditions [1] and with the influence of hepatic dysfunction [2] and of pregnancy.[3] The present paper is a complement to the last of the foregoing and deals with the influence of the level of ovarian activity. Previous studies in this field in which galactose was the test sugar [4] had demonstrated a very marked effect of the age and sexual status on the amount of the latter sugar susceptible of utilization by the organism. In the present instance, similar series have been studied, levulose of the highest purity being used, a necessary precaution; [1] for purposes of control the galactose tolerance has also been

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Dr. Rowe died, Dec. 6, 1934.

From the Evans Memorial, Massachusetts Memorial Hospitals.
Read before the Section on Pathology and Physiology at the Eighty-Fifth Annual Session of the American Medical Association, Cleveland, June 15, 1934.

1. Rowe, A. W.; McManus, Mary A., and Plummer, A. J.: The Metabolism of Levulose; 1. Some General Considerations on Provocative Levulosuria, Am. J. M. Sc. **188**: 15 (July) 1933.

2. Rowe, A. W.; McManus, Mary A., and Plummer, A. J.: The Metabolism of Levulose: IV. The Hepatic Influence on the Utilization of Galactose and Levulose, New England J. Med. **210**: 1163 (May 31) 1934.

3. Rowe, A. W.; McManus, Mary A., and Riley, G. A.: The Metabolism of Levulose: VII. The Influence of Pregnancy, read before the Annual Meeting of the American Physiologic Society, New York, 1934.

4. Rowe, A. W., and McGuinness, Mary: The Metabolism of Galactose: IV. The Effect on the Tolerance of the Level of Ovarian Activity, Am. J. Obst. & Gynec. **16**: 687 (Nov.) 1928.

determined. The general method of approach has already been discussed;[1] it may be enough here to state that each subject was given a thorough general clinical and laboratory survey, which included as a routine a careful physical examination, the compilation of an exhaustive medical history, analyses of the blood and urine, measurement of the respiratory metabolism,

TABLE 1.—*Composition of Groups*

Group	No. of Cases	Age Range	Average Age
Prepubescent	13	5-13 years	10 years
Pubescent	11	11-14 years	13 years
Adult	22	18-26 years	20 years
Castrate	15	21-51 years	34 years
Castrate with endocrine complication	4	55-60 years	57 years

and a variety of other tests and observations, among which were a cardiogram, an audiogram, a radiologic study and a neurologic examination.[5] As in the earlier studies, the Hofmeister[6] technic, i. e., the administration of successive graded doses, was followed; an exceeded tolerance was indicated by the appearance of detectable amounts of levulose[7] in the urine. A positive qualitative test was followed by a quantitative study, the Benedict[8] and Folin-Berglund[9] methods being supplemented by fermentation with washed yeast and by the polariscope. The complete analytic approach will be discussed in a forthcoming paper shortly. Earlier studies[1] have demonstrated the limitation of

TABLE 2.—*Normal Subjects*

Author	Dose	Levulosuria
Sabatowski, A. R.: Gaz. lek. **26**: 1291, 1907...	100 Gm.	0
Strauss, H.: Charité-Ann. **28**: 170, 1903.....	100 Gm.	0
Landsberg, G.: Deutsche med. Wehnschr. **29**: 563 (Aug. 6) 1903.....	100 Gm.	57%
Achelis, H.: Klin. Wehnschr. **8**: 641 (April 2) 1929	60 Gm.	9%
Jacoby, H.: Deutsche med. Wehnschr. **53**: 232 (Feb. 4) 1927.....	50 Gm.	0
von Noorden, Carl: Die Zuckerkrankheit, ed 5, Berlin, E. A. Hirschwald, 1910.....	1.7 to 2.1 Gm. per Kg.	
Goetsch, E.; Cushing, H., and Jacobson, C.: Bull. Johns Hopkins Hosp. **22**: 165 (June) 1911	100 Gm.	

the approach by the blood sugar curve method, particularly when levulose, with its slight influence on blood sugar levels, is the test sugar. While 10 Gm. differences were selected for the galactose program, the recognized higher tolerance of the organism led to the adoption of the larger interval of 25 Gm. for grading the levulose dosage. The general program can be shown most compactly in chart 1.

Modifications of this general scheme were easily applied to special cases, thus effecting a saving in time and in the costly sugar used for the study. The basic data of the several groups falling in this series are collected in table 1. Additional details are given in the discussion of the results with each of the several groups. The recognition of departures from the normal presupposes a definition of the latter quantity. As elsewhere noted,[1] there are but limited reports of normal studies in the literature, and the results recorded show a serious lack of concordance. The use of so-called hospital normals as test subjects and failure to make due allowance for the carbohydrate paradox (Allen) are unquestionably principal factors in producing this lack of agreement. A few data drawn from the literature serve to illustrate the conflicting evidence. The earliest papers derive from the studies produced by Strauss's[10] initial proposal to use levulose tolerance as a test for liver function; the two latest, the reawakened interest in the potentialities of this sugar for function testing.

Turning to the first study group, we have a series of thirteen normal children ranging in age from 5 to 13 years, none of whom had established the catamenia or indeed gave somatic evidence of an imminent approach of maturation. They were hospitalized during the study, and the more elaborate and detailed approach

TABLE 3.—*Prepuberal*

Datum	Variation	Average
Weight, deviation	+10% to −17%	−8%
Basal rate, deviation	+1% to −17%	−9%
Alveolar carbon dioxide	35 mm. to 43 mm.	39 mm.
Blood sugar	80 mg. to 107 mg.	93 mg.
Galactose tolerance	20 Gm.	20 Gm.
Levulose tolerance	75 Gm. to 100 Gm.	81 Gm.

designated as the "long form"[5] was utilized for the investigation of each case.

All these children had been previously institutionalized[11] to correct very poor social backgrounds, and the prevailing underweight of the group reflects these unfortunate earlier conditions. They were being most adequately provided for at the time of the transfer for this study, however, and as a further safeguard were given several days of liberal feeding[12] before the sugar testing was initiated. The basal rate levels were probably influenced by an earlier protein inadequacy associated with their undernutrition, although but one (−17 per cent) exceeded the conventional low limit of the normal. The prevailing level of alveolar carbon dioxide tensions was somewhat low throughout the group, and such levels we have found to be a rather common observation in similar groups of children. There is no evidence of an acidosis; it is possibly referable to their sexual status, but the question is one falling outside the present discussion. Blood sugars are normal; the galactose tolerance was uniformly at the level that the earlier studies have shown to be that of normal prediction. The levulose tolerance, i. e., initial positive response, was at either 75 or 100 Gm., the first

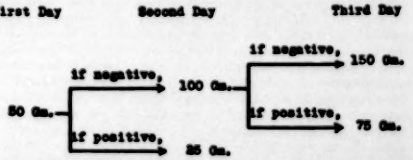

Chart 1.—Levulose program: additional doses at appropriate levels when first three days fail to give positive test.

5. Rowe, A. W.: The Differential Diagnosis of Endocrine Disorders, Baltimore, Williams & Wilkins, 1932, pp. 14-16 and 17.
6. Hofmeister, F.: Ueber die Assimilationsgrenze der Zuckerarten, Arch. f. exper. Path. u. Pharmakol. **25**: 240 (Feb. 21) 1888-1889.
7. Benedict, S. R.: A Reagent for the Detection of Reducing Sugars, J. Biol. Chem. **5**: 485, 1909. Seliwanoff, T.: Notiz über eine Frucht Zuckerreaction, Ber. d. deutsche Chem. Gesellsch. **20**: 181 (Jan. 25) 1887.
8. Benedict, S. R.: The Detection and Estimation of Glucose in Urine, J. A. M. A. **57**: 1193 (Oct. 7) 1911.
9. Folin, Otto, and Berglund, Hilding: A Colorimetric Method for the Determination of Sugars in Normal Human Urine, J. Biol. Chem. **51**: 209 (March) 1922.
10. Strauss, H.: Zur Funktionsprüfung der Leber, Deutsche med. Wchnschr. **27**: 757 (Oct. 31) 1901.
11. In these studies we are under especial obligation to the Home for Destitute Catholic Children, and in particular to Dr. John A Foley, under whose medical supervision these little patients fall.
12. Traugott, K.: Klin. Wchnschr. **1**: 892 (April 29) 1922.

predominating, as could be inferred from the reported average. The child organism is apparently able to utilize some four times as much of this hexose as of galactose.

The children in the next group (table 4) ranged from those who had just matured to those who had been menstruating for a number of months but all less

TABLE 4.—*Pubescent*

Datum	Variation	Average
Weight, deviation	−2% to +4%	−10%
Basal rate, deviation	−1% to (−25%)	−13%
Alveolar carbon dioxide	35 mm. to 38 mm.	37 mm.
Blood sugar	Not secured	
Number of periods	1 to 10	4
Galactose tolerance	20 Gm. to 40 Gm.	38 Gm.
Levulose tolerance	75 Gm. to 100 Gm.	89 Gm.

than one year. They were drawn from the same institution as the prepubescent children and the same conditions influencing weight had been operative with them. They too were hospitalized and had been given several days of preliminary feeding before the sugar tests were begun. Several of them had basal rates below the conventional limit of −10 per cent; the same earlier condition of a partial protein inanition obtained even more definitely in this group, as from their age they had been longer subjected to subversive nutritional influences. The one patient with marked lowering (−25 per cent) gave no evidence of other physical abnormality than that of underweight (−14 per cent). A thyroid failure could not be excluded in this single instance but, as this condition would have but little if any influence on the sugar tolerance, inclusion of the

TABLE 5.—*Young Adult*

Datum	Variation	Average
Weight, deviation	+40% to −16%	−2%
Basal rate, deviation	+9% to −19%	−6%
Alveolar carbon dioxide	39 mm. to 47 mm.	44 mm.
Blood sugar	80 mg. to 95 mg.	87 mg.
Galactose tolerance	40 Gm.	40 Gm.
Levulose tolerance	100 Gm. to 125 Gm.	105 Gm.

case is felt to be warranted. The low alveolar carbon dioxide has already received comment with the preceding group.

The galactose tolerance ranged from the prepuberal to the adult tolerance with rough correlation between sugar level and duration of the catamenia. Previous studies [4] already cited have shown that the adult level of 40 Gm. is usually attained by the end of the first year or shortly thereafter.

The levulose tolerance shows the same range as with the preceding younger group, but the average is higher, the 100 Gm. doses being more frequently encountered. In other words, levulose tolerance shows the same upward trend as does galactose, but in a much less marked degree and seemingly at a slower rate of change.

The group of young women [13] in table 5 were drawn from several sources, chiefly from the students in two women's colleges and a nurses' training school. They were studied initially under the program of the abridged type ("short form"),[5] supplemented by such tests and observations as the apparent needs of the individual case required. The one obese girl (+40 per cent) had a somewhat low sitting height index, so that the expression of her overweight is somewhat too high. She was a large framed powerful girl living an actively athletic life; her overweight was seemingly no more than a personal characteristic. Only two of the basal rates were significantly below conventional normal standards (−16 per cent, and −19 per cent), and in both a dietary tribute to current mores was probably the background, as both had low urine nitrogen elimination. They made the sacrifice, however, of an ample carbohydrate intake for several days before the sugar testing. The carbon dioxide tensions and blood sugar levels are normal both as to average and as to the individual measurements. The galactose tolerance was at the 40 Gm. level, which past experience has indicated to be the norm for the premenopausal female adult. Levulose tolerances likewise show a continuance of the upward trend manifested in the pubescent group, with 100 Gm. the common result but a sufficient number at 125 Gm. to exercise a modest effect on the average. We believe that both must be regarded as normal but

TABLE 6.—*Castrates: Recent, Two to Three Weeks*

Datum	Variation	Average
Weight, deviation	+43% to −29%	+1%
Basal rate, deviation*	−10% to −17%	−14%
Alveolar carbon dioxide	38 mm. to 46 mm.	41 mm.
Blood sugar	82 mg. to 97 mg.	88 mg.
Galactose tolerance	10 Gm. to 30 Gm.	22 Gm.
Levulose tolerance	75 Gm. to 125 Gm.	86 Gm.

* Incomplete.

that the lower level of 100 Gm. will be more frequently encountered among the normal, healthy adult group. While the averages for the three groups already discussed show an unmistakable upward trend, there is lacking among them those relatively sharp lines of demarcation which mark the progressive stadia of the galactose tolerance.

As has been noted in several of our previous papers, there is reason to conceive of a special influence of the mammary glands on the metabolism of galactose. Certainly both synthesis and storage of this sugar are implicit in lactation, and we have reported two small series of cases [14] in which patients after bilateral mastectomy, in which malignant neoplasm was ruled out, showed a decline of the galactose tolerance to the characteristic prepuberal level of 20 Gm. Levulose would not enter into any such selective mechanism and the

TABLE 7.—*Castrates Established, One to Eleven Years*

Datum	Variation	Average
Weight, deviation	+56% to −16%	+23%
Basal rate, deviation*	−12% to −32%†	−20%
Alveolar carbon dioxide	39 mm. to 45 mm.	42 mm.
Blood sugar	80 mg. to 104 mg.	97 mg.
Galactose tolerance	20 Gm.	20 Gm.
Levulose tolerance	25 Gm. to 150 Gm.	96 Gm.

* Incomplete.
† Low protein; later record −19 per cent.

present data offer some further support to the general hypothesis. In the second paper cited,[3] removal of the breasts produced no significant change in the response to levulose.

Whatever may be the true explanation, it must be recognized that while changes in the levulose tolerance show a rough qualitative agreement with those of galactose, quantitatively they are less significant and less sharply defined.

13. The authors are indebted to all who participated in these studies, in the case of the patients at no small inconvenience to themselves.

14. Rowe, A. W., and McGuinness, Mary: The Metabolism of Galactose: V. The Effect on the Tolerance of the Cycle of Reproduction, Am. J. Obst. & Gynec. 17: 351 (March) 1929. Rowe, McManus and Riley.[3]

Turning to pathologic material for an extension of the present thesis, the results of castration may next be considered. In dealing with individuals presenting this condition, however, extreme caution is needed in the interpretation of results. Residua of the influences which initially led to the operation may in themselves modify the sugar metabolism and the presence of significant and possibly independent complications arising at a later date must not be overlooked. For this reason the standardizing studies were made as comprehensive as possible; even with this precaution the need for conservatism in interpretation remains.

TABLE 8.—*Castrates With Endocrine Complication*

Datum	1*	2	3†	4	Average
Complication	T+	T+	T+	Pan	
Period of castration, years	16	15	16	4	12
Weight, deviation, per cent	—16	—31	+14	+32	
Basal rate, deviation, per cent	+51	+56	— 2	—10	
Alveolar carbon dioxide, mm.	42	39	46	39	42
Blood sugar, mg.	85	86	89	235	
Galactose tolerance, Gm.	10	10	10	10	10
Levulose tolerance, Gm.	100	125	100	25	

* Also bilateral breast amputation.
† Operated hyperthyroid.

The patients in this group (table 6) were examined immediately at the end of their convalescence following castration. Cystic ovaries and inflammatory pelvic conditions—in two instances only of a possibly specific origin—were the basis of the surgical intervention. The weight fluctuations reflect the status of the individual subject, some of whom were undoubtedly cases of functional hypogonadism prior to the operative confirmation of their endocrine status. The basal rates all show a downward tendency; the well known difficulty of securing basality in the case of ovarian failure is emphasized in this group with the added factor of the disturbance of a recent major operation. The carbon dioxide values are transitional and the blood sugars normal, as was to be anticipated. The galactose tolerance shows fluctuations both above and below the anticipated terminal level, though the average closely approximates it. The results with levulose practically duplicate those with the galactose, although no one test was inferior to the lower level observed in prepubescence. The average, 86 Gm., approximates that of the latter group.

The second group of castrates (table 7) is composed of a group of women whose ablating operation had taken place from one to eleven years prior to the time of study. With this group the establishment of compensatory adjustments and the development of later complicating and unassociated conditions are both factors to be borne in mind in evaluating the results. Broadly, the general data reflect the underlying condition. The tendency to obesity is more pronounced, the basal rate levels are more representative. The carbon dioxide tensions in the relatively normal average reflect a possible compensatory mechanism. The galactose tolerance is at the anticipated prepuberal level, an evidence of the probable absence of disturbing factors that might affect the metabolism of this sugar.

On the other hand, the levulose values show a very wide scatter from a point well below the normal low prepuberal tolerance to one superior to that of the normal adult. With so small a series as the present, a single extreme value exercises an undue influence on any average. For example, deleting the single high value (150 Gm.) lowers the average to 85 Gm., while if both of the extreme cases are omitted the average is at the wholly normal level of 100 Gm. Careful study of these individual cases failed to disclose any known reason for their profoundly altered levulose metabolism. The values can only be given as they stand with just recognition of the limitations imposed by so small a group.

One last small group may be added in which an ovarian failure of surgical origin is complicated by a known endocrinopathy involving another focus. Each case must be recorded separately, as there is lacking the necessary parity for collective presentation.

Patients 1 and 2 were castrates of sixteen and fifteen years' standing respectively, with a current hypothyroidism. In addition, in case 1 both breasts had been removed some two years previously for a nonmalignant condition. They both presented manifestations characteristic of the active thyroid status; the galactose tolerance was depressed to a 10 Gm. level; the levulose figures, on the other hand, were those of normal intact adults. Seven other cases of uncomplicated hyperthyroidism ranged from 25 to 125 Gm. with an average of 92 Gm. (unpublished data); the depressing effect of this condition on the galactose tolerance has been noted in several of our earlier papers. Patient 3 had been successfully operated on for a toxic thyroid some twenty years earlier, and four years later the ovaries had been removed. The normal basal rate may be a reflection of an algebraic compensation between a residual upward influence of the remaining thyroid tissue and the depression from the castration. The galactose level at 10 Gm. offers modest support for this interpretation. The levulose tolerance is again that of the normal adult.

Finally, case 4 was one of mild diabetes in which castration had been done four years previously. The galactose level is consistent with this double depressing influence, and here the levulose result is equally responsive to the pancreatic action. So low a level, however,

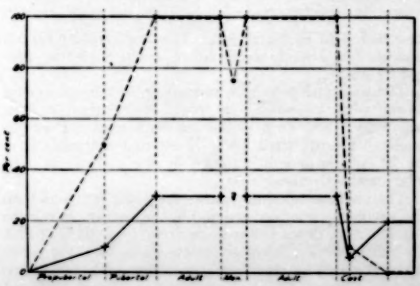

Chart 2.—Solid line, level of galactose tolerance; broken line, level of levulose tolerance.

is not to be regarded as characteristic, as a small group of patients with uncomplicated diabetes gave an average of 73 Gm. for their levulose tolerance (unpublished data).

COMMENT

In view of the running comment on each series, but little additional discussion is needed. Obviously the mechanisms of utilization of the two sugars are not identical, although both respond to certain agencies in kind though not in degree. The level of ovarian

activity, so potent in determining either directly or indirectly the utilization of galactose, is but qualitatively reflected in the changing levels of levulose metabolism. Castration produces a wide scatter in the levulose results, some of which are presumably mediated by agencies at present unknown and seemingly not operative in the metabolism of galactose. A clear-cut thyroid effect on levulose is not significantly indicated in the few available results.

With recognition of its limitations, the fluctuations of the two sugar tolerances may be diagrammatically presented (chart 2).

ABSTRACT OF DISCUSSION

DR. HENRY J. JOHN, Cleveland: This work presents an interesting problem, apparently new, the effect of the gonads on the metabolism of levulose. I found something of that sort in my studies of the dextrose tolerance work in the various endocrine groups, gonadal and otherwise. The metabolism of levulose was once considered to be largely a liver function. Here it is being found that there are other things which are affecting it and changing the picture. Extreme care must be used with regard to what is called a normal standard, a normal individual. If one goes over a small series of any type of test, one gets a certain impression. After one has multiplied that series 100 or 1,000 times, the picture usually changes extremely; sometimes one has just the opposite impression. The final word here, of course, will be said when the work has progressed still further and when more has been learned about the endocrine end of it as it affects the metabolism of levulose.

ALLERGY TO CHICLE

PRELIMINARY REPORT

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My object in this paper is to report the occurrence of allergic manifestations following the use of chewing gum. There has been no similar report, to my knowledge, in the literature.

CASE 1.—A. S., a white school boy, aged 16, seen in October 1933, complained that whenever he chewed gum he experienced attacks of sneezing, itching and swelling of the eyes, and occasionally spasmodic coughing. These symptoms generally set in within one half to three quarters of an hour after the gum was first taken and subsided about two hours after its removal. Subsequently he observed that, if he chewed gum more rapidly, the onset of the symptoms was accelerated.

The past history was that of the usual childhood diseases. There was no history of symptoms of the upper respiratory tract. The tonsils had been removed some years before. With the exception of the present complaint there was no previous history of any form of allergy or drug idiosyncrasy. His younger brother is under treatment for ragweed hay fever and food asthma, and his mother is subject to migraine.

The boy was well developed and nourished, was 5 feet 7 inches (170 cm.) in height and weighed 135 pounds (61 Kg.). The eyes were normal and the conjunctivae clear. There was no obstruction of the nasal passages, and the nasal mucous membrane appeared normal. There was evidence of tonsillectomy. Examination of the thorax showed the heart and lungs to be within normal limits. The blood pressure was 110 systolic and 80 diastolic. No abnormalities were noted.

In order to establish which constituent of chewing gum caused the allergic symptoms, its several ingredients were used in testing. Intradermal tests with milk and corn meal were negative. A drop of oil of peppermint (he was partial to this flavor), placed on the tongue did not result in any reaction. He was tested for salicylates because oil of wintergreen, which contains from 98 to 99 per cent of methyl salicylate, is used as a flavoring in some chewing gum. Acetylsalicylic acid was used for this test by having the patient ingest a five grain tablet and also by the method suggested by Duke.[1] The latter consists of placing several small specks of a tablet on the patient's tongue and allowing the alkaline juices of the saliva to break up the acetylsalicylic acid into sodium salicylate and sodium acetate. The reaction, if any, should occur within one minute. No reaction either immediate or delayed occurred in either instance.

The final substance to be investigated was chicle, and the boy was therefore tested with various extracts of both refined and crude chicle.[2] Three minutes after the introduction of concentrated chicle extract intradermally the patient commenced to sneeze, the spasms were progressively more violent, the conjunctivae became congested and he complained of severe itching of the eyes and was restless and irritable. Dyspnea and spasmodic coughing became evident and later edema of the eyelids was observed to be setting in. Locally, the sites of the intradermal tests showed wheals measuring 7 by 3 cm. in diameter with marked pseudopods. The reaction to the crude and refined chicle extracts appeared to be identical. Because of the severity of the reactions, weaker extracts (4 per cent) were then prepared and on a subsequent occasion the boy was retested with them. At this time the chronological sequence of the symptoms was carefully observed. Five minutes following the tests with the dilute extracts the boy complained of dizziness, which was followed in four minutes by itching of the eyes and sneezing. The latter symptoms, which came on about the same time, became progressively more severe in character. Fifteen minutes after the tests were introduced asthmatic breathing was noted, and twenty minutes afterward edema of the left lower eyelid. The latter became more marked gradually, involving also the upper lid. The wheals that occurred at the sites of the tests reached their maximum dimensions in fifteen minutes and exhibited marked pseudopodic processes. The most marked local reaction occurred from chicle that had been freed from the acetone-soluble fraction and dissolved in Coca's solution. The patient complained of marked itching of the arm around the wheals.

On both occasions, inspection by a nasal speculum revealed the mucous membrane of the nose to be edematous and the turbinates turgescent. The conjunctivae were also congested. On auscultation of the chest, sibilant and sonorous râles were heard. One cc. of epinephrine was required to control the severe symptoms following the use of the concentrated extracts, and 0.3 cc. when the dilute preparation was used. Ephedrine in combination with a sedative was prescribed to be taken at home, on account of the marked systemic reaction. The edema of the eyelids was the last symptom to disappear in both instances.

CASE 2.—M. R., a white man, aged 29, a dentist, seen, March 23, 1934, complained of a clogged nose, rhinorrhea ever since he could remember, and sneezing attacks with general aggravation of symptoms since December 1933. The rhinorrhea and sneezing were of such a severe character as to inconvenience him seriously and embarrass him in the practice of his profession. No antecedent family history was elicited, but his son, aged 3 years, had manifested urticarial eruptions on several occasions. The personal history was that of frequent "colds" all the year round as long as he could remember.

The patient had a mild tendency to obesity, was 5 feet 7½ inches (171 cm.) in height and weighed 168 pounds (76 Kg.). The nose was obstructed, the turbinates were markedly turgescent, especially on the right side, the septum was deviated and the mucous membrane was pale and boggy in appearance. The tonsils were out and there was no postnasal discharge. The heart showed no evident enlargement. The sounds were somewhat distant. The blood pressure was 110 systolic and 84 diastolic. The lungs were clear at the time of the examination and other physical manifestations within normal limits.

From the Allergy Department of the Beth-El Hospital, service of Dr. Louis Sternberg.

1. Duke, W. W.: Aspirin Allergy: A Method of Testing Aspirin Sensitiveness and a Method of Avoiding Aspirin Catastrophes, J. Allergy 5:426 (July) 1933.

2. The chicle used was obtained from the three main manufacturers of chewing gum in the United States. Two types of extracts were prepared for testing; one was crude or refined chicle in Coca's solution or distilled water; in the other type the chicle was first subjected to extraction with acetone, and the acetone undissolvable residue was extracted with Coca's solution or distilled water.

Intradermal tests were performed with the usual inhalants and foods. Orris root, 0.001 mg. of nitrogen per cubic centimeter of extract as determined with the Kjeldahl method, when introduced intradermally, resulted in a tremendous wheal about 6 by 4 cm. in diameter with pseudopods. Violent sneezing and rhinorrhea set in about three minutes after the test was introduced. Epinephrine was required to control the symptoms. Marked reactions were also obtained to some vegetables and fruits and also to timothy, but without systemic reactions.

Intradermal tests with extracts of chicle on another occasion resulted in very marked wheals similar to those in case 1 and approximating the patient's orris root reaction, including the nasal and asthmatic symptoms. Clinically it was difficult for him to note any effects from chewing gum, as he had been having nasal symptoms almost continuously.

Twenty-five other cases of allergic individuals, mostly cases of seasonal hay fever, and six nonallergic arthritic patients were tested with the concentrated extracts of chicle. Only one case exhibited a moderately positive local skin reaction, but no confirmatory clinical history was elicited.

Ordinary chewing gum has as its base chicle gum, into which are incorporated sugar, corn syrup and flavoring oils. The most common of the latter are wintergreen, peppermint and spearmint. One brand of chewing gum contains also milk. The formula varies with the manufacturer, but the base used in most cases is one or another variety of chicle.

Allergy to chicle is of interest because of its widespread use in the manufacture of chewing gum and medicated gums.

Chicle is the solidified latex or sap of one or more varieties of the species of the genus Achras trees.[3] The latter are native to Central and South American countries, notably southern Mexico, British Honduras and Guatemala. Achras zapota, a plant common in all tropical countries, is stated to be the source for the best grades of chicle. Most of the chicle imported into the United States comes from Mexico.

Chemically, chicle is a mixture of water-soluble gum, resins, gutta and mineral constituents. The composition, according to Dannerth,[4] is given in the accompanying table.

The chemical nature of the substance in chicle which produced the symptoms cited in our case is at present being investigated.

Composition of Chicle

	Per Cent
Resin (acetone soluble)	40
Gutta and carbohydrates	17.4
Proteins	0.6
Water	35
Ash	4.7
Foreign matter	2.3

Before the crude chicle is used in the manufacture of chewing gum, according to Roberts,[5] it is washed [6] and dried in separate chambers to reduce the moisture to approximately 4 to 6 per cent. The chicle is then heated until it flows freely and allowed to pass filters under 200 pounds of pressure to remove the fibrinous material. The purified gum is now passed into mixing kettles, where the sugar and flavoring oils are incorporated. Specialized automatic machines are used in producing from this mixture the final product ready for market.

3. These chicle-producing trees are known by different names in different areas. Thus in the Spanish-American countries they are called Nispero; in the British West Indies, Sapodilla; in Mexico and the Philippine Islands, Zapote chico.

4. Dannerth, Frederic: The Industrial Chemistry of Chicle and Chewing Gum, J. Indust. & Engin. Chem. **9**: 679 (July) 1917.

5. Roberts, S. G.: Making Chewing Gum for the Multitude, Compressed Air Magazine **7**: 3176 (July) 1930.

6. The exact meaning of the word "washed" could not be determined by the writer either from the literature or by communication with manufacturers. One manufacturer writes "The washings of some chicles entail the use of some agents which are used for the removal of some of the resins."

SUMMARY

Two cases exhibited marked positive local skin reactions when tested intradermally with extracts of chicle. In one case (case 1) Cooke's postulates [7] were satisfied. These require (1) that there should be a positive skin reaction with the suspected substance, (2) a history of exposure to the substance in question, and (3) the ability to reproduce the symptoms when the patient is exposed to it. The other case (case 2) presented obvious difficulties in establishing a positive clinical history. The marked positive skin tests, however, associated with systemic reactions, leads one to suspect strongly that this patient also had genuine chicle allergy.

It was also proved that chicle does not act as a skin irritant producing nonspecific reactions by the fact that out of twenty-five allergic patients only one showed a moderately positive skin reaction.

762 St. Marks Avenue.

7. Cooke, R. A.: Bronchial Asthma in Tice, Frederick: Practice of Medicine, section 3 Diseases of the Respiratory System, 5, Hagerstown, Md., W. F. Prior Company **5**: 497, 1921.

From Temple University School of Medicine and the Research Institute of Cutaneous Medicine of Philadelphia.

Aided by grants from the Daniel J. McCarthy Fund for Research in Neurology of Temple University and two anonymous donations.

1. Kolmer, J. A., and Rule, Anna M.: Am. J. M. Sc. **188**: 510 (Oct.) 1934.

2. Kolmer, J. A., and Rule, Anna M.: J. Immunology **26**: 505 (June) 1934.

A SUCCESSFUL METHOD FOR VACCINATION AGAINST ACUTE ANTERIOR POLIOMYELITIS

FURTHER REPORT

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As recently stated by Kolmer and Rule,[1] it is possible to vaccinate Macacus rhesus monkeys safely and successfully against acute anterior poliomyelitis with subcutaneous and intracutaneous injections of vaccines of living but attenuated virus composed of 4 per cent suspensions of poliomyelitic monkey spinal cord in sterile 1 per cent solutions of sodium ricinoleate. All of a series of eighteen monkeys were immunized sufficiently without the slightest evidences of ill effects to protect them completely against infection following the intracerebral injection of about eighteen minimal infective doses of virus given under ether anesthesia about one month after the last dose of vaccine, the disease developing in unvaccinated controls in from five to nine days after inoculation.

Following these observations, two of us received subcutaneous injections of 0.5, 1.5 and 2 cc. of the vaccine at intervals of five days without any ill effects whatever except local reactions at the sites of injection, and two weeks later our serums were found to contain large amounts of antibody in neutralization tests.

During the previous year, Kolmer and Rule [2] succeeded in vaccinating one monkey partially and two

additional animals completely, out of a series of six, with subcutaneous and intracutaneous injections of a vaccine of 2 per cent poliomyelitic spinal cord in 10 per cent sodium ricinoleate, so that the latter or stronger vaccine yielded much more satisfactory results with milder local reactions at the sites of injection, owing to the lower concentration of sodium ricinoleate.

Owing to the fact that it appears that living vaccines of attenuated viruses are more vaccinogenic than heat or chemically killed viruses, we employed sodium ricinoleate (William Merrell Company [2a]) as the attenuating agent not only because it is known to be detoxifying,[3] but likewise because McKinley and Larson [4] had successfully immunized three monkeys completely and one partially with intraperitoneal injections of sodium ricinoleate treated emulsions of monkey spinal cord virus. At least it would appear that vaccines of attenuated viruses produce immunity in much smaller amounts than "dead" viruses, with the added advantage that the viruses after injection are probably able to multiply many fold with continued antigenic stimulation as well as requiring the injection of smaller amounts of spinal cord protein and thereby resulting in less strain on the antibody producing tissues and less likelihood of producing allergic sensitization.

Furthermore, marked success in the case of poliomyelitis has followed vaccination of monkeys with subcutaneous and intracutaneous injections of living virus or mixtures of virus and immune serum; [5] but these have been considered too dangerous for the vaccination of human beings.

Susceptibility, attack rate, mortality and incidence of residual paralysis and other factors in acute poliomyelitis in relation to vaccination of human beings have been discussed elsewhere,[6] it being pointed out that susceptibility is so high in children and especially among those under 10 years of age that a safe and effective method of vaccination is highly desirable and especially in epidemics, although the majority of adults appear to possess adequate resistance. Even among the latter, however, vaccination is worthy of serious consideration during epidemics at least, since serum neutralization tests by different investigators with a group of 128 varying in age from 15 years and upward has shown about 24.7 per cent without demonstrable amounts of neutralizing antibody in the blood.

METHOD OF STUDY

During the last four months we have administered the vaccine to a selected group of twenty-five children varying in age from 8 months to 15 years, as summarized in the table, with completely negative histories of clinical attacks of poliomyelitis. All were immunized at the request or with the written consent of the parents, nineteen being in Temple University Hospital in the pediatric service of Dr. Ralph M. Tyson, to whom we are indebted for this cooperation. While all these children were in fairly good health, the majority were convalescing from various medical and surgical ailments.

Fifteen of these children were selected on the basis of showing no antibody in the blood by serum neutralization tests and ten with antibody in order to include both types in the study. These tests were conducted by mixing 0.5 cc. of serum with 0.5 cc. of a 10 per cent suspension of virus followed by intracerebral injection of 0.5 cc. of each mixture into monkeys under ether anesthesia after being allowed to stand about two hours in a water bath at 37 C. Control monkeys injected with 0.5 cc. of a mixture of 0.5 cc. of sterile saline solution and 0.5 cc. of virus after standing under identical conditions developed paralysis in from five to nine days.

Temperature observations and blood examinations were made in twenty-two of the children before and after each dose of vaccine.

From one to three injections were given subcutaneously at weekly intervals, the amounts of each being shown in the table.

Results of Administering Vaccine to Twenty-Five Children with Negative Histories

No.	Age	Name	Preliminary Serum Tests for Antibody	Dosage of Vaccine Once a Week, Cc.	Final Serum Tests for Antibody
1	8 mos.	Raymond B.	0*	0.25, 0.5, 0.5	0
2	9 mos.	Nickolas V.	0	0.5	+
3	10 mos.	Phillip B.	0	0.25, 0.5	+
4	12 mos.	Joseph W.	0	0.25, 0.5, 0.5	0
5	19 mos.	Howard N.	0	0.5	+
6	22 mos.	Francis B.	0	0.25, 0.5, 0.5	+
7	4 yrs.	Carolyn D.	0	0.5, 0.5, 1.0	+
8	4½ yrs.	Margaret Y.	+	0.5, 1.0, 1.0	++
9	5 yrs.	Philip D.	+	0.5, 0.5, 1.0	++
10	5 yrs.	Elizabeth M.	0	0.5, 0.5, 1.0	0
11	5 yrs.	Harry W.	0	0.5, 0.5, 1.0	0
12	6 yrs.	Gloria A.	+	0.5, 1.0, 1.0	++
13	6 yrs.	Joseph B.	+	0.5, 0.5, 1.0	++
14	7 yrs.	Charles D.	+	0.5, 1.0, 1.0	++
15	7 yrs.	Mildred G.	0	0.5, 1.0, 1.0	+
16	7 yrs.	Peter L.	0	0.5, 0.5, 0.5	+
17	7 yrs.	Elva W.	0	0.5, 0.5, 1.0	++
18	8 yrs.	Robert K.	+	0.5, 0.5, 1.0	++
19	8 yrs.	Clinton B.	0	0.5, 1.0, 1.0	+
20	10 yrs.	Kathryn D.	+	0.5, 1.0, 2.0	++
21	10 yrs.	Harold L.	+	0.5, 0.5, 1.0	++
22	11 yrs.	Sidney G.	+	0.5, 1.0, 1.0	++
23	11 yrs.	Daniel K.	0	0.5, 1.0, 1.0	+
24	11 yrs.	George W.	0	0.5, 1.0, 2.0	+
25	15 yrs.	John K.	+	0.5, 1.0, 2.0	++

* 0 indicates no antibody; +, antibody present; ++, antibody increased.

RESULTS OF VACCINATION

There were no ill effects in any of the children, and not the slightest evidences of infection. Local reactions of varying degree occurred at the sites of infection. In one of the older children the first dose produced a moderately severe reaction of swelling and erythema corresponding to that sometimes seen following injections of diphtheria toxoid, but in the remainder the local reactions were of mild degree.

During the first twenty-four hours after injection and especially after the first, the temperature of some of the children was elevated to a fraction of a degree but only occasionally going as high as 100.2 F. and falling to the preinjection levels in about forty-eight hours.

The total leukocytes were increased from 500 to 1,200 per cubic millimeter of blood in some of the children during twenty-four hours following injections and especially after the first, as the result of a slight absolute increase of the polymorphonuclear neutrophils. These and the slight temperature changes were

2a. We are indebted to the William Merrell Company for a generous supply of this substance (patent 1621118).

3. Larson, W. P., and others: Proc. Soc. Exper. Biol. & Med. **21**: 278, 1924; **22**, 194, 1924. Larson, W. P., ibid. **23**: 497 (March) 1926. Kolmer, J. A.; Rule, Anna M., and Madden, Bernard: J. Lab. & Clin. Med. **13**: 972 (June) 1934.

4. McKinley, J. C., and Larson, W. P.: Proc. Soc. Exper. Biol. & Med. **24**: 297 (Jan.) 1927.

5. Flexner, Simon, and Lewis, P. A.: Experimental Poliomyelitis in Monkeys, J. A. M. A. **54**: 1780 (May 28) 1910. Aycock, W. L., and Kagan, J. R.: J. Immunology **14**: 85 (Aug.) 1927. Stewart, F. W., and Rhoads, C. P.: J. Exper. Med. **48**: 959 (June) 1929. Rhoads, C. P., ibid. **51**: 1 (Jan.) 1930; **53**: 115 (Jan.) 1931.

6. Kolmer, J. A.: Susceptibility and Immunity in Relation to Vaccination in Acute Anterior Poliomyelitis, Am. J. M. Sc., to be published.

ascribed to the effects of the local reactions, as they appeared to vary with the degree of the latter.

Serum neutralization tests for antibody were conducted one week after the last dose of vaccine by mixing 0.5 cc. of serum with 0.5 cc. of a 10 per cent suspension of virus, allowing it to stand at 37 C. for but one to two hours, and injecting 0.5 cc. of each mixture intracerebrally into monkeys under ether anesthesia.

In the fifteen children without antibody before immunization, eleven, or 75 per cent, showed sufficient amounts of antibody to neutralize the virus after immunization, the monkeys showing absolutely no evidences of infection over three to four weeks following intracerebral inoculation of the serum-virus mixtures, while the controls inoculated with but 0.1 cc. of virus alone became paralyzed in from six to nine days and succumbed.

Since Brodie [7] has recently shown that the maximum immunity from two intracutaneous doses of poliomyelitis virus in monkeys is obtained by giving the second while the first is giving its effects, in other words, at intervals of from ten to fourteen days apart, it is quite likely that our injections at weekly intervals were too closely spaced and that even better results might have been produced by giving the injections at longer intervals. Furthermore, while antibody production in some of the children appeared to be quite prompt after injections of the vaccine, as will be discussed shortly in more detail, it is likely that serum neutralization tests for antibody should be delayed for at least two weeks after the last dose instead of but one week as conducted by us.

In addition it should be stated as previously mentioned that the majority of children included in this group were convalescing in the hospital from various medical and surgical conditions with the possibility that antibody response may not be as good under the circumstances as occurs in children in excellent general health.

Despite these conditions, however, the production of large amounts of antibody in eleven out of fifteen, or 75 per cent, of susceptible antibody-free children by from one to three doses of vaccine, with absolutely no ill effects other than the slight local reactions at the sites of subcutaneous injection, indicates a satisfactory and successful degree of immunization.

Furthermore, the serums of the ten children containing antiviral antibody in the blood before vaccination showed a sharp increase of antibody after immunization, since 0.5 cc. of serum mixed with as much as 0.5 cc. of 50 per cent suspension of virus followed by the intracerebral injection into monkeys under ether anesthesia of 0.5 cc. of the mixtures, after standing but one to two hours at 37 C., showed complete neutralization. Indeed, it would appear from additional quantitative tests that the vaccine probably produces more antibody in those children carrying natural antibody in the blood than it does in those who do not, suggesting that the body cells in the former are probably sensitized or "tuned up" by previous unrecognized infection with virus, with the result that they produce large additional amounts of antibody on additional stimulation by vaccine. At least twenty-one, or 84 per cent of the group of twenty-five children, showed good antibody response to the vaccine.

7. Brodie, Maurice: J. Immunology **27**: 395 (Oct.) 1934.

DOSAGE OF VACCINE

The matter of dosage is of course one of considerable importance. Monkeys receiving a total of 0.5 cc. per kilogram in divided doses by subcutaneous injection have been successfully vaccinated; [1] but, if it is true that human beings acquire immunity to poliomyelitis by clinically unrecognized infection with virus, it would appear that less vaccine may be required per body weight for effective immunization than in the case of monkeys.

With this possibility in mind and as an additional factor of safety, we have made the first dose 0.25 cc. for children under 3 years of age and 0.5 cc. for older children and adults. Second doses have varied from 0.5 to 1 cc. and third doses 1 or 2 cc., as shown in the table.

From the results observed up to the present time, it would appear that three doses are sufficient in the following amounts:

From 1 to 3 years: first, 0.25 cc.; second, 0.5 cc.; third, 0.5 cc.
From 4 to 10 years: first, 0.5 cc.; second, 0.5 cc.; third, 1 cc.
From 11 to 15 years: first, 0.5 cc.; second, 1 cc.; third, 1 or 2 cc.
Adults: first, 0.5 cc.; second, 1 cc.; third, 2 cc.

For children of standard weight the totals of these amounts of vaccine varied from about 0.06 to 0.1 cc. per kilogram, which were therefore approximately five to ten times less per body weight than given to monkeys. But we have assumed, as stated before, that human beings may require less than monkeys per kilogram of weight, and the results summarized in the table appear to substantiate this assumption. A possible exception was in the case of the two children (1 and 4) of 8 and 12 months respectively, who probably should have received 1 cc. for the third dose instead of 0.5 cc.; but otherwise we believe that the foregoing scale is about right in view of our present information on this subject.

However, it would appear that but one or two doses of vaccine have produced considerable antibody in at least some of the children.

For example, the serums of Nickolas V. (patient 2), aged 9 months, and Howard N. (patient 5), aged 19 months, gave good neutralization tests four days after one dose of 0.5 cc. Joseph W. (patient 4), aged 12 months, gave a good neutralization test one week after the second dose, although this result was not known when the third dose was given, and Clinton B. (patient 19), aged 8 years, also gave a good neutralization test four days after the first dose of 0.5 cc., although the second and third doses were also given before this result was known. These results indicate that with some children at least one or two doses may suffice; but since Raymond B. (patient 1), Phillip B. (patient 3) and Francis B. (patient 6) did not show antibody in the serums one week after the first dose, we believe it is advisable to give two and preferably three doses of the vaccine.

RAPIDITY OF ANTIBODY PRODUCTION AND SPACING OF INJECTIONS

In view, however, of Dr. Brodie's observations previously referred to on the rate of production of antibody in monkeys given subinfective doses of living virus intracutaneously, it would appear advisable to give the injections every ten days instead of every seven days as we gave them.

On the other hand, we have observed rather rapid antibody production in the cases just referred to,

namely, Nickolas V. (patient 2), Howard N. (patient 5) and Clinton B. (patient 19), since their serums taken ninety-six hours after the first dose of vaccine gave good neutralization tests. Indeed, in the case of Nikolas V., serum taken forty-eight hours after the first dose of vaccine appeared to contain already a very slight amount of antibody, as this monkey did not develop paralysis until eighteen days after intracerebral inoculation, whereas the control monkey and that tested with serum before vaccine was given developed severe paralysis thirteen or fourteen days after inoculation.

Further evidence of rather rapid antibody production was indicated by the fact that a monkey weighing 4 Kg. injected intracerebrally under ether anesthesia with 0.5 cc. of 5 per cent virus seventy-two hours after a subcutaneous injection of 0.5 cc. of vaccine remained perfectly well and entirely free of infection, whereas a control developed paralysis eight days after inoculation with but 0.1 cc. of the same virus given at the same time. In the case of a second monkey, however, receiving the same dose of vaccine, the antibody response, while present, was not quite as good, as this animal developed paralysis about nineteen days after the intracerebral injection under ether anesthesia of 0.5 cc. of the 5 per cent virus.

In this connection, observations on the rapidity of antibody production with the serums of individuals and monkeys with poliomyelitis are not without interest and some bearing on this question. Flexner and Amoss,[8] for example, have found antibody in the serum as early as the sixth day of the disease; Amoss [9] has found it in monkeys as early as three and one-half days after the onset of paralysis and in human beings as early as the fifth day; Leiner and von Wiesner [10] found it after seven, and in one case two days after the development of active disease in monkeys. Brodie [7] also found antibody in the blood of monkeys on the second day after the height of paralysis, while Howitt [11] failed to find it earlier than fifteen days after the onset of the disease in monkeys.

On the whole, therefore, it would appear that antibody may be produced rather rapidly in poliomyelitis and after subcutaneous injections of the vaccine, and for this reason we believe that vaccination may prove particularly helpful in the immunization of individuals during epidemics. Furthermore, as has been discussed elsewhere,[6] it does not appear that the vaccine produces a detectable "negative phase" or period of increased susceptibility in monkeys, at least, which also appears to justify its use in combating epidemics of poliomyelitis.

THE VACCINE

The method of preparing the vaccine has already been described [1] and need not be here given. Suffice it to emphasize that it is prepared of a remote monkey passage strain of the virus with the possibility of having lost at least some of its infectivity for human beings. That the antibody it produces is capable of neutralizing human virus [6] is indicated by the fact that the antibody in the serums of several of the vaccinated children was found to neutralize completely human virus from the 1934 epidemic in California sent us by Dr. Jessel of Los Angeles and a second virus in the third monkey transfer sent by Miss Howitt of San Francisco.

The vaccine, however, cannot be prepared of brain tissue because it contains insufficient virus. The intracerebral inoculation of monkeys with as much as 1 cc. of a 50 per cent suspension of fresh brain has failed to infect because virus was absent or present in insufficient amounts. But the spinal cord of one monkey will furnish about 150 cc. of vaccine, which is sufficient for the immunization of from forty to seventy-five children, depending on age and dosage.

We believe that the virus in the vaccine is attenuated to some extent by the amounts of sodium ricinoleate employed. While the intracerebral injection into monkeys under ether anesthesia of 0.1 cc. of 5 per cent fresh virus produced poliomyelitis in about eight days, the intracerebral injection of 0.2 cc. of a vaccine 3 weeks old and carrying 4 per cent of virus produced poliomyelitis in eleven days, while a second vaccine 2 months old produced paralysis in nine days and a third about 5 months old in about twelve days, all being injected in doses of 0.2 cc. under ether anesthesia.

The vaccine is allowed to stand at least two weeks before use and we now believe that a month may be better. After this time attentuation of the vaccine appears to stop when kept in the refrigerator at about 10 C., since vaccine prepared a year ago still possesses about the same infectivity for the monkey and the same vaccinogenic activity. In order to render different vaccines comparable in attenuated virus and immunizing activity, they are now prepared of mixtures of from ten to twenty cords taken only from monkeys that have been severely paralyzed.

In the preparation of the vaccine, due care must be exercised against contamination of the cords in removal and the preparation of finely divided suspensions. But it is our custom to place the cords in 50 per cent chemically pure glycerol in sterile saline solution for at least a month before use and under the circumstances the great majority of vaccines are found to be sterile on careful bacteriologic examination by culture.

The 1 per cent sodium ricinoleate possesses some bacteriostatic activity, but due care must be exercised against contamination of the vaccine when administered.

Since we have never seen the slightest ill effects, aside from mild local reactions at the sites of injection in monkeys or the twenty-seven human beings including two of us (J. A. K. and A. M. R.) who have taken it, we lost all fear of infection from its administration and are sure that it is perfectly safe. Unfortunately the monkey serum neutralization test is the only one available at present for the detection of susceptibility,[12] since skin tests,[13] colloidal gold, complement fixation and precipitation tests [14] have proved inadequate; but the majority of children under 10 years of age are devoid of antiviral antibody and probably susceptible, and since Aycock has shown that there is an important hereditary factor in susceptibility it would appear particularly important to vaccinate all children in those families in which the disease has appeared.

Not only is it quite likely that the remote passage virus employed has lost some if not all infectivity for human beings, but it is certainly attenuated to some extent by the sodium ricinoleate employed. Furthermore, subcutaneous injections appear to add another very important factor of added safety, as it represents a portal of entry in which virulent virus itself has a

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9. Amoss, H. L.: South. M. J. **23**: 18 (Jan.) 1930.
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14. Kolmer, J. A., and Rule, Anna M.: J. Immunology, to be published.

very low rate of infectivity for monkeys. In addition the injection of such a small first dose as from 0.25 to 0.5 cc. to children and adults and waiting at least a week before the second dose is given adds another important factor of safety, since it appears that antibody response is quite prompt. For these reasons we do not hesitate recommending the vaccine, especially during epidemics, and among the first children to receive it were the two sons of the senior author, the younger of whom was without any antibody at all in his serum before the first dose of 0.5 cc. was given.

SUMMARY

1. Twenty-five children varying in age from 8 months to 15 years have been given from one to three injections of poliomyelitis vaccine at the request or with the consent of parents.

2. Fifteen of these children were without antibody in serum neutralization tests before immunization and eleven, or 75 per cent, showed large amounts of antibody in the blood one week after the last dose of vaccine.

3. Ten of the children showed the presence of antiviral antibody in the blood before immunization, but all have shown a considerable increase of this antibody after vaccination, so that antibody production occurred in twenty-one, or 84 per cent, of the group of twenty-five children.

4. None of the twenty-five children have shown the slightest ill effects from the vaccine.

5. Mild local reactions were produced at the sites of subcutaneous injection, with occasional slight elevation of temperature and slight leukocytosis subsiding within forty-eight hours.

6. The dosage for children from 1 to 3 years of age has been 0.25, 0.5 and 0.5 cc. at weekly intervals; for children from 4 to 10 years, 0.5, 0.5 and 1 cc.; for children from 11 to 15 years, 0.5, 1 and 1 or 2 cc. For adults the dosage recommended is 0.5, 1 and 2 cc.

7. The vaccine is prepared of spinal cord only, as brain contains too small amounts of virus. But the spinal cord of a single monkey will furnish about 150 cc. of vaccine, which is sufficient for the immunization of from forty to seventy-five children, depending on age and dosage.

8. It is likely that the maximum antibody response may be obtained by giving the injection every ten days instead of weekly.

9. Antibody production, however, appears to be fairly rapid, as three susceptible children developed antibody in the blood within four days after the first injection of vaccine and one monkey was found completely and a second partially immune seventy-two hours after the subcutaneous injection of 0.5 cc. of vaccine per animal on intracerebral inoculations of large amounts of virus.

10. The vaccine does not appear to produce a demonstrable "negative phase" of increased susceptibility after injection.

11. The vaccine is a 4 per cent suspension of spinal cords of monkeys developing poliomyelitis after intracerebral inoculation with a remote passage strain of virus, in a 1 per cent sterile solution of sodium ricinoleate prepared as previously described. The virus is attenuated and the vaccine regarded as entirely safe for the immunization of human beings not only because prepared of remote passage virus which probably has lost in infectivity for human beings but likewise because of attenuation by sodium ricinoleate, the route of administration and the injection of a small first dose.

12. The amount of antibody produced by immunizations is comparable to that found in the blood in natural immunity and is believed to be sufficient for affording protection against acute anterior poliomyelitis.

13. The antibody present in the serums of vaccinated children has successfully neutralized human virus from the 1934 California epidemic.

14. The duration of the immunity following vaccination is unknown but has lasted for more than two years in vaccinated monkeys.

15. It is believed that the vaccine is now ready for vaccination of human beings and especially children against poliomyelitis and particularly during epidemics.

Clinical Notes, Suggestions and New Instruments

LYMPHOBLASTOMA WITH PARAPLEGIA AND PROLONGED IRRADIATION

L. F. Wheatley, M.D., New Haven, Conn.

This case of lymphoblastoma (Hodgkin's type) is reported because of a number of points of unusual interest: certain neurologic and skin manifestations, its response to radiation therapy over a considerable period of time, and the changes found at autopsy.

The patient first came under my observation at 12 years of age with a negative family history and negative past history until 9 years of age, when she had mumps in the left parotid gland. A year later there was an enlarged cervical gland on the same side, which was removed surgically. A year later there was a recurrence, which was again operated on. At this time it was considered tuberculous and the patient was referred to a tuberculosis sanatorium, where routine examination of the chest disclosed a large superior mediastinal growth, corresponding to Wessler's group I—expanding mediastinal tumor. A recurring cervical gland enlargement was excised at this time and microscopic examination showed it to be a slow growing lymphoblastoma of the Hodgkin's type, which thus identified the mediastinal growth. At this time then, three years after her first glandular involvement, she was referred to me for radiation therapy. She was given heavily filtered high voltage (180 kilovolts) radiation over the upper mediastinum, anteriorly and posteriorly, approximately a 40 per cent depth dose into the tumor mass, and moderate voltage (125 kilovolts) with a filter of 3 mm. of aluminum over the cervical gland. The mediastinal growth entirely disappeared following this treatment.

She remained well for five years, when gastro-intestinal symptoms and a slight rise of temperature occurred, which I thought due to probable mesenteric lymphoid involvement. Chest examination showed some recurrence of the mediastinal tumor mass, which promptly receded again under radiation therapy.

A year later she developed partial paraplegia, exhibiting great difficulty in walking, and numbness from the shoulders down. I considered this evidence of the extension of the mediastinal growth into the spinal cord and pressure on the nerve exits from the vertebral bodies. Roentgen examination showed no erosion of the vertebral bodies. Heavy (200 kilovolts) irradiation was again done over the upper dorsal spine, 860 roentgens being administered through each of two oblique portals within a week. Three months later she reported herself able to swim and to walk a mile with the aid of a cane, and her numbness was nearly gone. Six months after the onset she was apparently in a normal condition again. During this time she had two cycles of therapy similar to the one described. She remained well for nearly a year longer, when she again returned with aggravation of all the symptoms. At this time

she also had an aggravated case of herpes zoster, completely encircling the body on the level with the twelfth dorsal vertebra, which left deep scars. Radiation directed over the spine again relieved the gastro-intestinal symptoms, but the condition gradually grew worse. A laminectomy was considered to relieve pressure on the cord, but she was in very poor condition and I did not feel justified in taking the risk. Complete paralysis and anesthesia of both extremities, paralytic ileus, and urinary and fecal incontinence with ascending urinary infection developed, and the patient died.

AUTOPSY

When the chest cavity was opened, the left lung was seen to be adherent with numerous adhesions to the entire lateral wall and to the diaphragm, with more dense adhesions about the apex. The entire chest contents, including the mediastinum and heart, were removed *en masse*. The heart was small, and the pericardium was adherent to the epicardium throughout the thin, easily separated fibrous adhesion, which left the epicardium smooth but remained as tags on the pericardium. There were numerous various sized lymph nodes scattered all along the spinal column retroperitoneally, and one large calcified lymph node in the mesentery of the small intestine. The spinal cord was exposed and completely removed from the fourth lumbar vertebra to the brain. Beginning at the level of the sixth dorsal vertebra and extending to the last cervical vertebra was an extradural tumor mass adherent to the dura and extending out between the ribs on the right side, most markedly in the third interspace, but also in the second and fourth interspaces. This mass was entirely extradural and undoubtedly caused pressure on the cord. Opening of the dura, however, revealed no internal involvement whatever, and grossly the cord appeared perfectly normal. The tissue extending between the third and fourth ribs was excised and extended through to the pleural cavity, with no apparent bulging or involvement of the pleura itself. A single lymph node in the right neck was removed, which on gross examination showed hemorrhagic mottlings.

Microscopic examination of sections of the node removed from the neck showed a cellular structure with large areas of necrosis. The cells were of a size suggesting those of the germinal centers of a lymph node. On occasion, larger multinucleated cells were seen; also in places there was some fibrous tissue and a few eosinophils were present. The normal architecture of the lymph nodes had disappeared. A retroperitineal lymph node was quite similar but gave the impression of a more rapidly growing structure. An occasional dividing nucleus was seen. The extradural growth from the spinal canal and the extension out from that showed a similar picture as regards the type of cell present, but there was more fibrous tissue here than was seen of the lymph node described.

In my opinion the picture in this tissue and of the lymph node is to be explained as a chronic lymphoblastoma. Sections from the scar tissue in each apex of the lung showed compact fibrous tissue such as might have resulted from an old tuberculous process, though no tubercles were present to make such a diagnosis definite. The spinal cord showed no evident degeneration.

COMMENT

Paraplegia occurring in the course of Hodgkin's disease is a relatively well known condition, although few autopsy records have been reported. The response of such cases to irradiation are less well known, or at least less frequently reported. It is of interest to note the initial response to irradiation, which held it in check for nearly a year in this case. The mediastinal mass and the extension into the spinal canal had been reduced to fibrous tissue and it was the pressure of this mass confined within an inelastic bony chamber that produced this paraplegia. It is fair to presume that if the patient had been in any condition to withstand a laminectomy she might have survived for a considerable period longer.

In a review of the literature, Paullen[1] reports four cases of lymphogranuloma of the central nervous system, with extension by the way of the intervertebral foramen and destruction of the vertebral bodies with discrete growth in the epidural tissue of the spinal cord. There was temporary response to radiation treatment.

Parkes Weber[2] reports that there are very few definite cases with autopsy confirmation on record and but few with a history of improvement after high voltage radiation therapy.

Johnston[3] describes two types of spinal involvement: (*a*) degeneration of the cord due to anemia with resulting interference of the blood supply, and (*b*) pressure atrophy due to perineural infiltration. He states that most cases show compression myelitis from crushing of the bony canal or massive infiltration of the cord by granulomatous tissue.

Weil[4] reports forty-three cases with spinal cord involvement in which 85 per cent showed this as due to granulomatous tissue; in 80 per cent the thoracic segments were involved, in 16 per cent the cervical, and in 4 per cent the lumbar. There was no prolongation of life because of roentgen treatment, although he advocated early irradiation and laminectomy.

Cooper[5] reported a case proved at autopsy of direct extension of this lymphogranulomatous tissue from an extradural tumor, with extensions by the way of the nerve roots to the subdural space.

In the case here reported, it was found at autopsy that lymphogranulomatous tissue reached the vertebral canal by direct extension from the mediastinal tumor mass by way of the intervertebral foramen and that there was no actual destruction of the cord but the extension into the subdural space produced symptoms by compression only.

The occurrence of herpes zoster has been reported by Craven and Haagensen[6] as the expression of the involvement of the nervous system by granulomatous tissue, and they conclude that herpes zoster was caused by the new growth surrounding and compressing the ganglions corresponding to the peripheral areas involved. This conclusion was based on the autopsy.

Keichline[7] states that in every case this is a trophic expression of inflammation corresponding to the ganglion of the posterior roots, either spinal or cranial.

The blood Wassermann was 4+ and precipitation test (Kahn) was 3+, confirmed on several examinations. The father's and mother's blood were both negative on repeated examinations. The occurrence of repeated positive Wassermann reactions is of considerable interest. Moore, in his textbook of Modern Treatment of Syphilis, acknowledges a nonspecific positive occurring in certain conditions, such as malignant cachexias, glandular tuberculosis and yaws. The apparent close relation between Hodgkin's disease and tuberculosis suggests that Hodgkin's disease might possibly be included in this list. On the other hand, other syphilologists feel that there is a congenital syphilis in these cases and that repeated negatives in the parents indicate a spontaneous cure. In the present case there was a history of the father having been treated with mercurial inunctions when a youth, but there is no further history bearing on this point. The autopsy was entirely negative for any evidence of syphilis, and there had never been any clinical evidence suggestive of this condition.

SUMMARY

A case of lymphoblastoma was observed over a period of ten years and kept under almost complete control by roentgen therapy up to three months before the patient's death. The recurring mediastinal growth was held in check and finally reduced to a small mass of scar tissue. The developing paraplegia also responded to irradiation and almost complete relief of symptoms for a period of one year, and I believe might further have been controlled had the patient's condition justified a laminectomy. The patient developed an aggravated case of herpes zoster and showed a persistent Wassermann reaction without clinical or autopsy confirmation.

420 Temple Street.

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AN OBSTETRIC RING FOR ARTIFICIAL PUNCTURE OF THE MEMBRANES

Irving F. Stein, M.D., Chicago

Artificial puncture of the membranes is the simplest of obstetric operations. When one observes the awkwardness with which the operation is performed by inexperienced physicians and the amount of unnecessary trauma sometimes inflicted in attempting to rupture the membranes, the need for a simple, effective and harmless instrument becomes obvious.

The ring that I have devised is made of malleable metal so that it can be fitted to the gloved forefinger just behind the first joint. A rigid, notched projection extends along the dorsum of the first phalanx with the point directed to the inner aspect of the fingernail. When the finger is introduced into the vagina, the projection lies flat against the gloved finger, so that no trauma is inflicted on the mucous membrane of the vagina or on the cervix. Examination of the cervix and of the presenting parts may be made by means of the palmar surface or the tip of the finger, and when puncture of the membranes is indicated the finger is bent slightly, releasing the notched projection. The puncture is readily accomplished by rotating the finger mediad. The finger is again straightened and further examination of the presenting parts may be made to verify the position and to feel for a prolapsed cord, an extremity, and so on. Furthermore, the finger is in a favorable position to control the rate of escape of the liquor.

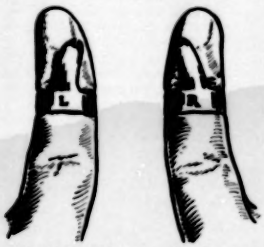

Fig. 1.—Obstetric rings for fingers of right or left hand.

The disadvantages of previous methods employed for artificial rupture of the membranes are as follows: 1. The notched finger-nail described by Edgar, appropriated from the ancient midwife, is obviously antiquated by the universal use of rubber gloves and is no longer approved by obstetricians. 2. The notched thimble requires a separate introduction of the finger into the vagina after the diagnosis has been made and a decision reached that the membranes shall be ruptured. The touch

Fig. 2.—*A*, palpation of bag of waters with palmar surface of finger; *B*, method of rupturing bag of waters with author's instrument, by bending and rotating finger.

surface of the finger is obliterated by the thimble. 3. Blunt or sharp forceps, scissors or crochet hooks require a separate insertion into the vagina and also carry the danger of trauma to the cervix and to the presenting part of the fetus.

The obstetric ring here described may be worn for every vaginal examination whether or not it is needed. It is light in weight and does not interfere with the vaginal touch or cause trauma. Thus the necessity of a second insertion of the finger or of an instrument is obviated if a decision is made to puncture the bag of forewaters. The obstetric ring has been tested in the Michael Reese Hospital maternity for several months, during which time it has been employed by members of the attending and house staffs with entire satisfaction. It may be obtained for use on either the right or the left hand according to the habit of the individual physician.[1]

From the Northwestern University Medical School and Michael Reese Hospital.

DEVICE FOR PROTECTION OF THE TEETH DURING BRONCHOSCOPY AND ESOPHAGOSCOPY

Sidney Israel, M.D., Houston, Texas

Protection of the upper teeth is one of the important factors in the technic to be observed during a bronchoscopic or esophagoscopic examination. There have been numerous occurrences of injury to the upper teeth, regardless of what instrument or method has been employed.

Unless the teeth have been properly protected, patients frequently complain of sensitiveness or tenderness of the teeth, particularly on the edges, lasting for several days after a bronchoscopic or esophagoscopic examination, as a result of the pressure of the metal tube, which rests on the edges of the teeth.

Heretofore to protect the upper teeth from injury by the bronchoscopic or esophagoscopic tube it has been the accepted

Rubber protector in place over upper teeth, ready for introduction of the bronchoscopic or esophagoscopic tube.

custom to use the examiner's thumb or a pad of gauze or cotton. Neither of these measures is completely satisfactory. When the thumb of one hand is used, that hand is eliminated so far as the execution of any operative manipulation is concerned. When gauze or cotton is employed to protect the upper teeth, the bulk either obstructs the mouth or is easily displaced.

For the purpose of protecting the upper teeth and safeguarding them from any injury or discomfort following an endoscopic examination, flexible rubber tooth guards were devised to cover the upper teeth. The endoscopic tube rests on the rubber guards over the teeth, rendering both hands free for the performance of any necessary operative procedure. These rubber protectors have accomplished the purpose for which they were designed and have proved very successful.

In order to arrive at standard or universal sizes, the mouths of a number of children and adults, as well as edentulous individuals, were examined. From these three classifications an average was obtained, and from these averages molds were made which represent standard sizes in the three classifications (1) child, (2) adult and (3) edentulous. The three sizes of tooth guards, as the result of their flexibility, will conform to fit all mouths belonging in their respective class. They offer no obstruction or curtailment to instrumentation, remain in

1. Manufactured by Sharp and Smith, Chicago.

Presented at the meeting of the American Academy of Ophthalmology and Otolaryngology at Chicago in September 1934.

place, and completely protect the teeth from injury. They can be easily cleaned or sterilized and are quickly applied or removed.

Aside from the protection offered through this medium of safeguarding the patient's teeth, it does much to eliminate any medicolegal controversy that may arise.

These tooth protectors are available through the Electro-Surgical Instrument Company of Rochester, N. Y.

2010 Esperson Building.

Special Articles

GLANDULAR PHYSIOLOGY AND THERAPY

INTRODUCTION

MORRIS FISHBEIN, M.D.
CHICAGO

In 1924 a series of articles—published in book form the following year and revised in 1927—was prepared under the auspices of the Council on Pharmacy and Chemistry of the American Medical Association with the general title "Glandular Therapy." In a brief introduction to that series Dr. Frank Billings emphasized certain significant factors in relationship to our knowledge of the glands which at that time many endocrinologists considered as established but which to some physiologists and clinicians were not quite acceptable. The points to which he referred concerned the alleged reciprocal action of the glands of internal secretion; i. e., the idea that the glands represent an interlocking chain of structures correlated in their activities through hormones carried in the blood stream. This led to the view that the entire functioning of the body might be stimulated, retarded or perverted by hyperfunction, hypofunction or alleged dysfunction of the ductless glands. It seems reasonable to believe today that the endocrinologists have established this view. In 1927, when the revised edition of "Glandular Therapy" was published, evidence was still fragmentary. Today it is more elaborate but, of course, only a beginning has really been made in our knowledge of this exceedingly complex and fascinating field.

One of the reasons why the Council on Pharmacy and Chemistry took up the subject specifically in 1924 was the tremendous abuse already evident in the use of preparations of glandular materials promoted by pharmaceutical manufacturers who were willing to exploit such preparations on slight evidence. Notwithstanding the fact that evidence was already available at that time to indicate that most glandular materials could not become effective in the human body when taken by mouth, manufacturers offered tablets, powders and solutions to be taken orally, representing every tissue in the body that might even remotely be assumed to elaborate something in the nature of an internal secretion. The tonsil, the kidney, the spleen and the heart as well as the tissue of the brain were included in such mixtures. One manufacturer even went so far as to prepare a series of revolving wheels on which were indicated various symptoms and a long series of numbered glandular preparations, the suggestion being that a summation of the symptoms would lead invariably to a glandular preparation of a certain number. Such obvious charlatanism could not long survive, particularly in the face of exact knowledge, which began to be accumulated. True, there are still some manufacturers who exploit preparations without scientific basis and with equally mysterious methods, but the majority of the medical profession seem to realize the folly of such therapeutics.

In 1927 there was but little in glandular therapy actually established. The entire volume made a book of some ninety-eight pages. There was evidence as to the usefulness of epinephrine and of the extract of the posterior pituitary. There was some usefulness indicated for thyroxine, thyroid gland tissue, insulin and parathyroid material, but beyond these there was little indeed that could be considered worth while. A comparison of that series of articles with the thirty contributions listed below as the constituents of the present series will indicate how interesting a road has been traveled in the intervening period. The concluding chapters of the book issued in 1927 dealt with the ovary and the mammary gland. The conclusion was then reached that ovarian therapy was wholly experimental and that there seemed to be little established, yet laboratory investigators indicated certain definite possibilities for the future. Mammary gland preparations were rejected entirely. In the present series of articles great emphasis is placed on the urinary, pituitary and placental gonadotropic factors. This pituitary-gonad relationship has led to conceptions of remarkable significance for clinical medicine.

Since 1927 the pituitary gland has been discovered to be a veritable storehouse of hormones. In addition to the growth hormone discussed by Evans and the gonadotropic principles considered by P. E. Smith, Collip speaks of diabetogenic, thyrotropic, adrenotropic and parathyrotropic factors. Riddle discusses the lactogenic factor, and Zondek the chromatophorotropic principle. The corpus luteum still constitutes a field for hopeful study rather than for any established therapeutic agent. Particularly significant from the discoveries of recent years have been those related to the estrogenic and gonadotropic substances and the application of such studies to the diagnosis of pregnancy. These, together with the work on the cortex of the adrenal, the thymus, the parathyroid and the testis, represent new phases of endocrinology that were hardly mentioned in the previous series.

The scope of research is today exceedingly broad. Hardly a month passes without an announcement of significance. Indeed, the progress is so rapid that it is hardly likely that another seven years will pass before a new edition, including many new facts and suggestions, will be required. Since it is of the greatest importance that clinicians be aware of what is established and what is still theoretical in this important field, the Council on Pharmacy and Chemistry has rendered another distinguished service in making available this series of articles.

These articles are part of a series published under the auspices of the Council on Pharmacy and Chemistry. Other articles will appear in succeeding issues of THE JOURNAL.

Dr. Morton S. Biskind of the headquarters staff of the Council outlined the general series and assisted in editing the articles toward uniform expression and avoidance of excessive duplication.

The articles in the new series include:

Clinical Manifestations of Dysfunction of the Anterior Pituitary. H. M. Evans, M.D., University of California.

General Physiology of the Anterior Hypophysis. P. E. Smith, Ph.D., Columbia University.

Growth Factor of the Anterior Pituitary. H. M. Evans, M.D., University of California.

The Hypophyseal Gonadotropic Hormones. P. E. Smith, Ph.D., Columbia University.

Interrelationships Among Urinary, Pituitary and Placental Gonadotropic Factors. J. B. Collip, M.D., McGill University.

Lactogenic Factor of the Pituitary. Oscar Riddle, Ph.D., Cold Spring Harbor.

Diabetogenic, Adrenotropic, Thyrotropic and Parathyrotropic Factors of the Pituitary. J. B. Collip, M.D., McGill University.

Anterior Pituitary and Anterior Pituitary-Like Substances—Therapeutic Applications. Emil Novak, M.D., Johns Hopkins University.

Chromatophorotropic Principle of the Pars Intermedia of the Pituitary. Bernhard Zondek, M.D., Jerusalem, Palestine.

Posterior Hypophysis. E. M. K. Geiling, M.D., Johns Hopkins University.

Physiology of Estrogenic Principles. Edgar Allen, Ph.D., Yale University.

Estrogenic Hormones and Carcinogenesis. Leo Loeb, M.D., Washington University.

Therapeutic Applications of Estrogenic Preparations. Emil Novak, M.D., Johns Hopkins University.

Corpus Luteum. G. W. Corner, M.D., University of Rochester.

Menstruation. Edgar Allen, Ph.D., Yale University.

Sex Endocrine Factors in Blood and Urine. R. T. Frank, M.D., Mount Sinai Hospital, New York.

Pregnancy Tests. Selmar Aschheim, M.D., University of Berlin.

Testis Hormone. C. R. Moore, Ph.D., University of Chicago.

Physiology of the Thyroid. David Marine, M.D., Montefiore Hospital, New York.

Pathogenesis and Prevention of Goiter. David Marine, M.D., Montefiore Hospital, New York.

Therapeutics of the Thyroid. J. H. Means, M.D., Harvard University.

Physiology of the Parathyroid. A. M. Hanson, M.D., Faribault, Minn.

Parathyroid Hormone Therapy. J. C. Aub, M.D., Harvard University.

Adrenal Medulla. J. M. Rogoff, M.D., University of Chicago.

Adrenal Cortex. Robert F. Loeb, M.D., Columbia University.

Thymus. L. G. Rowntree, M.D., Philadelphia Institute for Medical Research.

The Internal Secretion of the Pancreas. C. H. Best, M.D., University of Toronto.

Therapeutic Applications of Insulin. E. P. Joslin, M.D., Harvard University.

Liver and Stomach Preparations (Antianemic). Randolph West, M.D., Columbia University.

Gastro-Intestinal Principles. A. C. Ivy, M.D., Northwestern University.

CLINICAL MANIFESTATIONS OF DYSFUNCTION OF THE ANTERIOR PITUITARY

HERBERT McLEAN EVANS, M.D.
BERKELEY, CALIF.

Correct conceptions in almost every phase of the whole field of medicine rest on advances in experimental physiology. Belief in this view has been so well justified by the achievements of the last century that one may well claim the actual inauguration of modern medicine by the life work of such an investigator as Claude Bernard.

Endocrinology, a more or less well recognized clinical specialty, already possesses in some portions of its realm sufficiently precise and quantitative procedures for diagnosis and therapy, but in its other territories such tools are frequently so wofully lacking as to have led to a widespread feeling of insecurity in the field as a whole. Not only has a clinic of endocrine diseases been born in the last few decades, but a host of skilfully contrived and fruitful laboratory studies has been given to the world; the present moment is an appropriate one for inquiry as to the aid given clinical endocrinology by the results of modern experimental biology. The series of articles in THE JOURNAL of which this is the first is devoted to this end.

The experimental biology of the last decade, which has been directed toward securing both overfunction and underfunction of the pituitary gland, has now finally given adequate grounds for belief in the existence of at least five separate internal secretions or hormones of the anterior pituitary: the somatotropic,[1] the gonadotropic,[2] the thyrotropic,[3] the mammotropic,[4] and the interrenotropic[5] hormones. It is felt that the relation of these achievements to clinical medicine will be disclosed most successfully by the discussion of pituitary and related diseases with reference to the existence of proved deficiency or excess of these five known substances, for the recognition of which there are now specific tests.

I. GROWTH HORMONE

Underproduction.—*Dwarfism:* The first solidly won achievement of experimental research in the pituitary field may be described as the production of dwarfism and sexual infantilism following hypophysectomy in young animals, especially puppies. Mammals are unable to continue to increase in skeletal dimensions after hypophysectomy. The surprising stasis in the growth of the long bones can be confirmed in a few weeks by roentgenograms. They are similarly unable to increase their body substance strikingly, as determined by postoperative weighings.[6]

From the Institute of Experimental Biology, University of California.

For collaboration in this work the author is indebted to his associates Drs. Miriam E. Simpson, W. R. Lyons and E. H. Rynearson.

1. Somatotropic hormone: the growth hormone, phyone, antuitrin G, somatotropin.

2. Gonadotropic hormone: gonad-stimulating hormone, glandular hebin, sex hormone of the anterior lobe, gonadotropin.

3. Thyrotropic hormone: thyreotropic or thyroid-stimulating hormone, thyrotropin.

4. Mammotropic hormone: lactogenic hormone, mammary-stimulating hormone, galactin or prolactin, mammotropin.

5. Interrenotropic hormone: adrenotropic, adrenalotropic or adrenocorticotropic hormone, interrenotropin.

6. In cases in which the hypophysectomy has injured the contiguous hypothalamus, adiposity may result (Camus and Roussy; Smith), and it is to be borne in mind that weight increases after a complete hypophysectomy may be thus explained. Selye states that a slight and temporary capacity for growth is present if the hypophysectomy has been done on very young animals.

Cases of human dwarfism due to defective function of the anterior lobe have been designated by Erdheim as nanosomia pituitaria. It is not improbable that any and all forms of dwarfism are directly caused by inadequate pituitary function, regardless of the ulterior cause. Cretinic dwarfs are apparently the result of the depression of pituitary function due to thyroid subnormality, and restoration of their growth can be effected either by the administration of thyroid (which can be understood to stimulate the hypophysis) or by direct treatment with pituitary extracts.

The growth of hypophysectomized rats or puppies can be readily produced by the use of anterior lobe extracts; these may now be freed sufficiently from contaminating hormones as to produce normal growth, while the thyroids, sex glands and adrenal cortex remain atrophic.[7]

The classification of human dwarfism is not completely satisfactory at the present time. Part of the difficulty is due to the fact that the defective growth may or may not be associated with sexual infantilism. Diminutive individuals with adult proportions exist; more often the childhood proportions are retained, the upper length of the body exceeding the lower. The latter cases are usually sexually delayed or infantile. In some of them a peculiar, unexplained, senile appearance manifests itself (progeria).

Human dwarfism has been treated with pituitary extracts by several careful workers [8] who have reported that children who had ceased growth, or were growing at a subnormal rate, resumed normal growth or even exceeded the growth rate normal for the age at treatment.

Deficiency of Growth Hormone in Adult Life: It has thus far been impossible for the experimentalist to eliminate the growth hormone only, either in infantile or in adult life; nor are there adequate grounds for believing that in human hypopituitary states only the growth hormone has been eliminated. In 1914 the Hamburg pathologist E. A. Simmonds reported a cachectic and rapidly wasting state associated with the finding at necropsy of complete destruction or sclerosis of the pituitary. Animals deprived of the pituitary frequently develop a similar cachectic state. Our reason for believing that the growth hormone is not concerned here rests on the fact that, although such animals can be forced to grow with growth hormone extracts, the cachexia continues. The cachexia is relieved by crude anterior lobe extracts but not by adrenal cortical extracts, so that it has no affinities with Addison's disease.

The rôle of the growth hormone in adult life is thoroughly obscure. The return of hair over shaved areas is speedier in its presence than in its absence. Brugsch (1927) has described a disease, akromikrie, which he considers the converse of acromegaly. It is characterized by thinning of acral parts, subnormal growth, falling hair, thirst, amenorrhea and acrocyanosis.

The growth hormone is not more abundant in the anterior lobes of young calves than in those of adult cattle, and it is certain that the hormone is employed in the physiologic mechanism of the body throughout life.

Overproduction.—*Gigantism and Acromegaly:* Clinicians felt secure in the interpretation that general symmetrical overgrowth (gigantism) and also an asymmetrical disfiguring overgrowth in adult life (acromegaly) were both due to overactivity of the anterior hypophysis. The pituitary was found to be hypertrophied in both conditions; in acromegaly the gland is enlarged, essentially owing to increase of the eosinophilic cells.[9] Any insecurity in this interpretation may be said to have ended with the experimental production of gigantic rats and of acromegalic dogs.

No source for growth hormone preparations other than anterior lobe tissue itself has yet been discovered. The hormone has not been recognized as yet in the blood or urine in acromegaly, nor has the claim of its presence in the urine of pregnancy been substantiated.

II. GONAD-STIMULATING HORMONES

In 1926 Zondek and Aschheim and, independently, P. E. Smith discovered that anterior pituitary tissue implanted under the skin or intramuscularly in immature rats or mice brought about a development of the ovaries and other signs of precocious sexuality within four days. The ovarian picture was complex. Along with typical follicular growth, ovulation and the formation of corpora lutea there occurred a premature lutein transformation of the walls of many ovum-containing follicles. The growth of the ovarian follicles is now referred to a specific one of the two gonadotropic hormones which it is thought are secreted by the pituitary gland. It has been called "the follicle-stimulating hormone." The development of lutein tissue is regarded as an effect of another gonadotropic substance—"the luteinizing hormone." [10] Zondek and Aschheim quickly extended their discovery to the domain of clinical medicine by detecting gonadotropic hormone in the urine of pregnancy; later they found gonadotropic substance in body fluids and tissues in other conditions. These authors early showed that predominantly follicle-stimulating effects were produced by the principle found in menopause urine [11] but that these were combined with luteinizing effects when pregnancy urine [12] was given. The Berlin investigators unfortunately spoke of both urinary substances as anterior lobe substances, and much confusion in the literature has been created thereby. The gonad-stimulating substance present in pregnancy urine does not exactly resemble any chemical fraction that has been hitherto secured from anterior lobe substance; a long series of studies, beginning with that of Evans and Simpson in 1929, has shown it to be less efficacious than pituitary implants

7. P. E. Smith (Increased Skeletal Effects in A. P. Growth-Hormone Injections by Administration of Thyroid in Hypophysectomized, Thyroparathyroidectomized Rats, Proc. Soc. Exper. Biol. & Med. **30**: 1252 [June] 1933) has shown that an enhanced growth of such animals can be obtained by simultaneous administration of thyroid extracts with such preparations.

8. Shelton, E. K.; Cavanaugh, L. A., and Evans, H. M.: Hypophyseal Infantilism: Treatment with Anterior Hypophyseal Extract; Preliminary Study, Am. J. Dis. Child. **47**: 719 (April) 1934. Engelbach, W.; Schaefer, R. L., and Brosius, W. L.: Endocrine Growth Deficiencies; Diagnosis and Treatment, Endocrinology **17**: 250 (May-June) 1933.

9. This was first recognized by Benda (1900) and securely established by the studies of Fischer (Die Beziehungen des Hypophysentumors zu Akromegalie und Fettsucht, Wiesbaden, Bergmann, 1920) and of Bailey and Cushing. The histophysiology and histopathology of the anterior hypophysis is in a thoroughly unsatisfactory state. Such previously well established concepts as "pregnancy" and "castration" cells are either now denied validity or described as differing in different animal forms.

10. The ovarian effects of gonadotropic substances from various sources and from various treatments of anterior lobe tissue are not yet completely understood. The terms "follicle-stimulating" and "luteinizing" may turn out to be somewhat inappropriate when more is learned of their mechanism of action.

11. Menopause urine: prolan A, follicle-stimulating urine, castration prolan, castration urine.

12. Pregnancy urine: prolan, chorionic prolan, pregnancy prolan, urinary bebin, antuitrin S, follutein.

or extracts of whole anterior lobe substance. Some of these differences are that:

1. It cannot stimulate the growth of follicles and corpora in the ovaries of hypophysectomized animals.[13]

2. It does not affect the development of the immature avian testis. This is readily produced by anterior lobe substance.[14]

3. It has only slight effects on the monkey ovary—effects that do not lead to reddening of the sexual skin. This is produced by anterior lobe substance.[15]

4. When administered to normal immature rats, no matter how frequently or in what doses, it rarely produces ovarian weights in excess of from 40 to 70 mg. in ninety-six hours, whereas with anterior lobe substance increased effects are secured with increasing dosage, the ovaries attaining from two to three times the weight stimulated by pregnancy urine.[16]

Struck by the ineffectiveness of the gonadotropic substance in pregnancy urine in hypophysectomized animals and its partial effectiveness in normal immature ones, Evans, Simpson and Austin extracted anterior lobes in various ways in order to discover the substance needed to make the factor in pregnancy urine maximally effective. They designated this hypophyseal substance the "synergist." When combined with the gonad-stimulating principle of pregnancy urine, normal gonadotropic effects were secured even in hypophysectomized animals.[17] It is highly interesting that Leonard and Smith,[18] by the simple addition of the principle in menopause urine to that in pregnancy urine, have secured similar results. A chemical separation of anterior lobe extracts into follicle-stimulating and luteinizing components was at least partially made and announced as early as 1930 by Fevold, Hisaw and Leonard. Wallen-Lawrence[19] has also successfully fractioned anterior lobe substance into extracts with similar effects. Fevold and Hisaw[20] have recently suggested that their follicle-stimulating hormone is identical with the synergist shown to be essential for completing the action of the gonadotropic factor of pregnancy urine.

It would appear, therefore, that in the menopause and in pregnancy the body fluids contain types of gonadotropic hormone that are similar to, if not identical with, types that can be secured by chemical treatment of the pituitary gland. Combinations of either urinary component with the complementary gland component behave synergically. More than this cannot be said at the present time, nor will it be well to hazard a guess as to the identity of substances still incompletely known both biologically and chemically.

There are reasons for believing that the gonadotropic factor of the urine of pregnancy arises through the function of chorionic tissue and is not a product of the anterior hypophysis. These are that:

1. The chorionic tissue of the placenta has large amounts of gonadotropic substance in it, as demonstrated by implantation or injection of extracts, whereas the anterior lobe of women dying in pregnancy has little or no gonadotropic hormone in it (Philipp).

2. The same hormone is present in high amounts in all types of chorionic tissue growth, especially hydatidiform mole and chorionepithelioma, whether in women or in men.

3. A rare case of hydatidiform mole has been described in which the body fluids were singularly lacking in this substance. Study of the uterine wall showed that the mole had been delimited from the maternal circulatory system by a massive fibrin boundary zone, conceivably preventing leakage of the hormone shown to be actually abundant in the mole tissue.[21]

4. The hormone content is high in the chorionic villi of extremely young ova as well as in the body fluids before the hypophysis shows histologic pregnancy changes.

For all these reasons it would seem best to designate this substance as chorionic gonadotropic hormone.[21a] Admittedly the proof of its production by the chorion, without contribution by the pituitary, could be secured only by quantitative studies of its secretion in a pregnant hypophysectomized monkey. It is almost certain that the placenta likewise manufactures the massive quantities of estrogenic substance produced in pregnancy.[22]

The substance found in the blood stream and urine in underfunction of the ovary, in the menopause and following castration is certainly a product of the anterior pituitary. It would now appear certain that even the particular cells of the anterior lobe forming and storing this hormone are known—the basophils. The chain of evidence here is as follows:

1. The anterior lobe of castrated rats contains as a new feature the peculiar, enlarged signet-ring basophils or castration cells.

2. Such pituitaries contain an increased content of gonadotropic hormone.

3. The parabiotic union of a hypophysectomized female with a castrated male leads to the development of constant estrus and the presence exclusively of large follicles in the ovary of the female parabiont.[23]

Follicle-stimulating urine and the hypophyseal synergist have both been administered to hypophysectomized male rats, and it is highly interesting that in both cases there occurred marked stimulation of the germinal tissue (the seminiferous tubules) without stimulation of the interstitial tissue or accessory sexual apparatus. In the male, these particular gonadotropic substances are hence quite purely gametogenic in their effects and without influence on the secretion of the testis hormone by the Leydig cells, whereas other anterior lobe extracts or chorionic gonadotropic hormone affect the testicular interstitial tissue and accessory organs predominantly.

Inadequacy of gonadotropic hormones.—Hypophysectomy in young animals invariably leaves them sexually infantile; in fact, regression occurs from the stage of development of the genital system encountered

13. Reichert, F. L.; Pencharz, R. I.; Simpson, Miriam E.; Meyer, Karl, and Evans, H. M.: Ineffectiveness of Prolan in Hypophysectomized Animals, Proc. Soc. Exper. Biol. & Med. **28**: 843 (May) 1931.

14. Riddle, Oscar: Studies on Pituitary Function, Endocrinology **15**: 307 (July-Aug.) 1931.

15. Engle, E. T.: Biological Differences in Response of the Female Macacus Monkey to Extracts of the Anterior Pituitary and of Human Pregnancy Urine, Am. J. Physiol. **106**: 145 (Oct.) 1933.

16. Evans, H. M., and Simpson, Miriam E.: A Comparison of the Ovarian Changes Produced in Immature Animals by Implants of Hypophyseal Tissue and Hormone from the Urine of Pregnant Women, Am. J. Physiol. **80**: 381 (July) 1929.

17. Evans, H. M.; Pencharz, R. I., and Simpson, Miriam E.: The Repair of the Reproductive System of Hypophysectomized Female Rats by Combinations of a Hypophyseal Extract (Synergist) with Pregnancy-Prolan, Endocrinology **18**: 601 (Sept.-Oct.) 1934; Maintenance and Repair of the Reproductive System of Hypophysectomized Male Rats by Hypophyseal Synergist, Pregnancy-Prolan and Combinations Thereof, ibid. **18**: 607 (Sept.-Oct.) 1934.

18. Leonard, S. L., and Smith, P. E.: Ovarian Response of Hypophysectomized Rats to Urinary Follicle-Stimulating Principle, Proc. Soc. Exper. Biol. & Med. **31**: 283 (Nov.) 1933.

19. Wallen-Lawrence, Z.: Proof of the Existence of a Follicle-Stimulating and a Luteinizing Hormone in the Anterior Lobe of the Pituitary Body, J. Pharmacol. & Exper. Therap. **51**: 263 (July) 1934.

20. Fevold, H. L., and Hisaw, F. L.: Interactions of Gonad Stimulating Hormones in Ovarian Development, Am. J. Physiol. **109**: 655 (Oct.) 1934.

21. Philipp, E.: Blasenmole mit negativer Schwangerschaftsreaktion, Zentralbl. f. Gynäk. **55**: 491 (Feb. 21) 1931.

21a. Or chorionic gonadotropin.

22. Hart, G. H., and Cole, H. H.: The Source of Oestrin in the Pregnant Mare, Am. J. Physiol. **109**: 320 (Aug.) 1934.

23. Witschi, E., and Levine, W. T.: Oestrus in Hypophysectomized Rats Parabiotically Connected with Castrates, Proc. Soc. Exper. Biol. & Med. **32**: 101 (Oct.) 1934.

at the time of operation. Human infantilism is doubtless also in a large majority of cases referable to hypopituitarism. A satisfactory beginning has already been made in its treatment with gonadotropic hormones,[24] especially in delayed sexual development and cryptorchidism [25] in boys.

The relations between the pituitary and gonads are such that, while proper functioning of the latter may be prevented by inadequate secretion of the pituitary gonadotropic hormones, these hormones in other cases may be produced in normal amounts, but the gonads fail to respond. One can thus justifiably speak of primary and secondary hypogonadism. In the former case the gonad itself is at fault, as shown by abundant pituitary gonadotropic secretion in the blood stream; in the latter the pituitary gonadotropic function is at fault. The diagnosis is facilitated in women by the fortunate circumstance that both ovarian (estrogenic) and pituitary (gonadotropic) hormones are normally present in low amounts in the blood and urine after puberty.[26] Primary and secondary amenorrheas can therefore often be clearly segregated. Mazer and Goldstein ascribe some 80 per cent of cases of amenorrhea to hypophyseal insufficiency.

Gonadotropic therapy in amenorrhea, which will be more fully dealt with in a special article in this series, has on the whole been disappointing. As had been mentioned in the treatment of hypogonadism in the male, this has been largely due to the almost exclusive employment of the hormone found in the urine of pregnant women.

Underfunction of the hypophysis is not always expressed in the female as amenorrhea. It would appear from the successful results of therapy with the gonad-stimulating factor of pregnancy urine that Schroeder's disease (characterized by hypertrophic endometrium and excessive bleeding) may be the result of deficiency of gonadotropic hormone. The situation is further explained by the view that only one of the two hypophyseal gonadotropic hormones normally secreted is deficient, namely, the luteinizing hormone. The excessive amount of estrogenic substance produced by the cystic follicles undoubtedly causes endometrial proliferation, and an interruption of its production leads to the profuse uterine bleeding that characterizes these cases. The improvement resulting from the administration of gonadotropic substance is apparently due to its luteinizing power. At any rate, the cysts or large follicles characterizing the ovaries of these women are luteinized by the treatment and the condition in the uterus, and consequent excessive bleeding is corrected. Long continued amenorrhea may be present in such cases if there is no intermission in the outpouring of estrogenic substance from the cystic follicles present. Such an amenorrhea has been described recently by Zondek; exactly the same conditions were found in the ovary and the uterus as in metropathia hemorrhagica.

Overabundance of gonadotropic hormone.—*Pregnancy:* It is now well known that an outstanding characteristic of human pregnancy is the abundance in the blood and urine of estrogenic substance and of a gonadotropic hormone probably derived from the chorion. The increased quantity of estrogenic principle in these fluids appears somewhat later than does the rise in amount of gonadotropic hormone, though the estrus-inducing hormone lasts until birth, at which time it very abruptly diminishes. The gonadotropic hormone, on the other hand, is already abundant in the urine by the first missed period, constituting the well known Aschheim-Zondek test for pregnancy, a practically infallible means of recognizing gestation. The hormone reaches its maximum in the urine around the fourth or fifth month of pregnancy (from 5,000 to 20,000 mouse units per liter). The Aschheim-Zondek test has yielded outstanding service in the recognition of extra-uterine pregnancy. In the toxemias of pregnancy, extremely high amounts have been encountered in the last third of gestation.[27]

Parturition: At birth, gonadotropic hormone disappears promptly from the maternal urine, even though this may not take place with such spectacular suddenness as the withdrawal of estrogenic substance. One thousand mouse units per liter of gonad-stimulating hormone has been found in the first day or two of the puerperium, though it is reported absent by the tenth to the fourteenth day. A continuing high titer in the puerperium is always associated with retained membranes. The same phenomenon is seen with death of the fetus, but failure to expel it, in earlier stages of pregnancy.

Hydatidiform Mole and Chorionepithelioma: Very extraordinary titers are given with the hydatidiform transformation of the chorion, and in chorionepithelioma amounts of from 100,000 to 520,000 mouse units per liter have been reported. The complete removal of the mole or malignant tissue usually leads to rapid disappearance of the hormone, but a few cases have been reported in which the hormone lingered unduly. These cases have been used to support the hypothesis of the formation of the hormone by the pituitary itself. The argument is unconvincing. Besides reservoirs for the very temporary storage of gonadotropic substance, the possibility of metastases which later regress must be considered. Should the test remain positive after a mole has been passed or removed, it must be repeated every fortnight until negative, and thence once a month for, say, three times, for malignant transformation may come late. If the test should continue to be positive a

24. But it is unfortunate that the majority of the reported cases concern only the employment of the principle in pregnancy urine. This substance, as disclosed further in the present paper, is markedly limited in its gonadotropic effects in all animals and especially in primates.

25. Rubinstein, H. S.: The Production of Testicular Descent with the Water Soluble (Anterior Pituitary-Like) Fraction of Pregnancy Urine, Endocrinology **18**: 475 (July-Aug.) 1934. Sexton, D. L.: Treatment of Sexual Underdevelopment in the Human Male with Anterior Pituitary-Like Hormone of Urine of Pregnancy, ibid. **18**: 47 (Jan.-Feb.) 1934. Goldberg, M. W.: Treatment of Pituitary Infantilism with Antuitrin, ibid. **18**: 233 (March-April) 1934.

26. P. Wirz (H. V. H. und Amenorrhöe, Ztschr. f. Geburtsh. u. Gynäk. **104**: 293, 1933) finds only follicle-stimulating hormone in the urine of small children, the luteinizing factor appearing first at puberty; to its appearance he attributes the onset of the cycle. In men the quantity is extremely small (Evans, H. M.; Simpson, Miriam E., and Austin, P. R.: The Recognition and Comparison of Prolan and Prolan-like Substances, J. Exper. Med. **59**: 561 [Nov.] 1933. Katzman, P. A., and Doisy, E. A.: The Quantitative Determination of Small Amounts of Gonadotropic Material, J. Biol. Chem. **106**: 125 [Aug.] 1934) but in women the quantity is large enough to be demonstrable at moderate dosage of the alcohol precipitate out of urine. Zondek says that on the average 5 mouse units per liter is present. Frank and his co-workers (Frank, R. T.; Goldberger, M. A., and Spielman, Frank: Present Endocrine Diagnosis and Therapy, J. A. M. A. **103**: 393 [Aug. 11] 1934) find a definite variation with the cycle, a full mouse unit not being present in 40 cc. of blood until seven days before onset of the menses. (Estrogenic substance is found by them also to vary; increased excretion occurring about the tenth day and again about three days before onset of the next menstrual flow, about 1,200 to 1,500 mouse units being excreted per month.) Kurzrok and his associates (Kurzrok, R.; Kirkman, I. J., and Creelman, M.: Studies Relating to the Time of Human Ovulation, Am. J. Obst. & Gynec. **28**: 319 [Sept.] 1934) describe a definite rise in gonad-stimulating hormone in blood just preceding or at the time of ovulation, on days 10 to 13 of the cycle.

27. Heim, K.: Ergebnisse quantitativer Hormonanalysen bei Schwangerschaftstoxikosen, Klin. Wchnschr. **13**: 1614 (Nov. 10) 1934.

month after removal of the uterus for definite chorionepithelioma, one may be sure of the growth of metastases.

It is in cases of mole and chorionepithelioma that the hormone is found in the cerebrospinal fluid; it is not detectable in the liquor in normal pregnancy.

Testicular Tumors: Testicular tumors of particular types (the classic work is Chevassu's), which are now recognized as teratoid though they possess undifferentiated or embryonal cells (embryonal carcinoma and sometimes true chorionepithelioma), also give astonishingly high amounts in the urine. We have ourselves seen a case in conjunction with Hinman and Powell in which the urine shortly before death contained one million rat units per liter. Several cases of retroperitoneal and mediastinal locus of these tumors with complete freedom of both testes have now been reported. As in malignant transformation of the chorion in the female, the following of the titer in the urine is important as indicating local or metastatic recurrence.

Castration, Hypogonadism and the Menopause: It has been found that women who for any reason have partial or complete loss of ovarian function often [28] excrete considerable amounts of castration gonadotropic hormone; e. g., after the menopause, after operative removal of the gonads, after roentgen castration or after hypogonadism resulting from pathologic processes in the gonads. Other amenorrheas due to unexplained ovarian insufficiency and the amenorrhea of lactation belong here. Zondek, Wirz and others agree that urinary titers of more than 100 mouse units per liter indicate absence of function of the ovary. Österreicher [29] finds from 80 to 300 mouse units per liter in the urine in both castration and the menopause. The hormone is also found in the urine of castrated men.

Genital Cancer: Zondek's early studies convinced him that malignant tumors of the genital tract were three or four times as prone to be associated with the presence of urinary gonadotropic hormone as were benign growths. In fact, he felt that some indication of the malignancy of a genital neoplasm could be secured by implanting fragments of the tumor tissue into immature rodents; if strongly positive, malignancy was indicated. But neither this procedure nor the titration of urines for gonadotropic hormone has yielded the same spectacular service in genital cancer afforded by similar tests of the body fluids in mole and chorionepithelioma.

Miscellaneous Conditions with Increased Hormone: Riley and his associates [30] have shown the presence of the menopause hormone in the urine in migraine, its appearance being correlated with the seizures. Kraus [31] has shown the hormone in cases of brain tumor and in 60 per cent of women with increased intracranial pressure. In skin diseases, e. g., pruritus vulvae and acne rosacea, the urinary hormone has also been reported.

III. LACTOGENIC HORMONE

The invariable association of milk secretion with reproduction in the female was itself an a priori reason for supposing that the hormone characteristic of pregnancy, that of the corpus luteum (progestin), was responsible for the mammary changes. Yet it would appear that nothing is better established than the nonconcern of lutein function with mammary activity. The latter is now known to be due primarily to the secretion of another special hormone (prolactin, or the lactogenic hormone) by the anterior lobe. Experimental biology may be said to have demonstrated:

1. The necessity of estrogenic substance [32] to provide the growth stimulus to the mammary gland.
2. The fact that the estrogenic factor is limited in its effects—it causes an unfolding of the duct system but not development of secretory alveoli.
3. The non-necessity of progestin [33] in mammary physiology.
4. The invariable dependence of the mammary gland for functional development on prolactin.
5. The inhibition of prolactin secretion by estrogenic substance.

It is probably safe to say that all mammary glands have been exposed to estrogenic hormone, even if only temporarily, during fetal life and immediately post partum. The majority of new-born infants show a mammary growth spurt, and often secretion, following the elimination of estrogenic substance from the system in the first week of life. The preliminary action of estrogenic hormone, its withdrawal or diminution, followed by a temporary prolactin secretion, would seem to explain the long debated phenomenon of witch's milk.

The cyclic changes in the breast showing maximum development, and often secretion, at the time of menstruation have as their best explanation a cyclic secretion of prolactin. Cases have been described wherein milk is secreted regularly during menstruation or in place of menstruation, at the usual intervals.[34] The fact that breast growth and lactation may follow ovariectomy or the menopause forces one to the conclusion that continued stimulation by estrogenic substance is not necessary to the breast and that prolactin may continue to be effectively secreted long after the influence of the estrogenic factor has disappeared. Cows lactate for two years following ovariectomy, and women have been known to do so for several months. The stripping of these spontaneously lactating glands would probably prolong lactation by virtue of a reflex prolactin secretion [35] as well as by preventing regression due to alveolar stagnation. The fact that one fourth of all women show parenchymal breast hypertrophy following the menopause, instances of senile lactation, cases of prolonged lactation (especially those associated with amenorrhea, uterine regression or fibroid) point to hypersecretion of prolactin or at any rate to a prolactin effect, which to some extent may be due to the removal of the inhibition exercised by estrogenic substance.

In pregnancy or pseudopregnancy, a gradual continuous growth of the breasts is substituted for the cyclic changes. The fetus plays no important rôle, if

28. Some claim that 100 per cent of old women will be found to have a hormone in their urine if repeated examination is made.

29. Österreicher, W.: Vermehrte Ausscheidung von Hypophysenvorderlappenhormon (Prolan) im Harne in der Involutionsperiode bzw. im Senium, Klin. Wchnschr. **11**: 813 (May 7) 1932.

30. Riley, H. A.; Brickner, R. M., and Kurzrok, R.: The Abnormal Excretion of Theelin and Prolan in Patients Suffering from Migraine, Bull. Neurol. Inst., New York, **3**: 53 (June) 1933.

31. Kraus, E. J.: Zur Genese der kleincystischen Degeneration der Ovarien, Arch. f. Gynäk. **152**: 383, 1933.

32. A generic term used throughout this series to avoid the confusion entailed by the current employment of its many alleged synonyms. The reader is referred to an editorial, "The Nomenclature of Glandular Products" (THE JOURNAL, Oct. 13, 1934, p. 1152), in which this subject is discussed.

33. Progestin: corporin, hormone of the corpus luteum.

34. Schweitzer, B.: Zu der Wechselbeziehung zwischen Genital- und Mammafunktion, Zentralbl. f. Gynäk. **47**: 717 (May 5) 1923. Gauthier, neveu: Un cas de secretion lactée remplacant les règles chez une jeune fille vierge, Lyon med. **100**: 199, 1903. Landau, L.: Ueber einige Anomalien der Brustdrüsensekretion, Deutsche med. Wchnschr. **10**: 743, 1890. Landau described a nullipara who lactated in place of menstruation for one and a half years following double ovariectomy.

35. Selye, Hans: On the Nervous Control of Lactation, Am. J. Physiol. **107**: 535 (March) 1934.

any, in mammary physiology and the chorion probably need only be considered because of its contents of estrogenic and gonadotropic hormones. Guinea-pigs and women may continue pregnancy and deliver and suckle their young following ovariectomy,[36] but if an animal is hypophysectomized during pregnancy the mammary growth is inhibited, and even though a small amount of milk may be present after parturition the breasts quickly atrophy.[37] It is not unlikely that prolactin is alone responsible for the growth of the breast in pregnancy and in the puerperium, since with prolactin one may obtain full development and lactation in animals ovariectomized after reaching sexual maturity.[38] Estrogenic substance depresses prolactin secretion during pregnancy; the expulsion of the placenta, whether at term or prematurely, releases that inhibition, and full growth of the breasts and lactation follow.[39] Failure to lactate following parturition may in some instances be explained by an excess of estrogenic substance in the system or simply by insufficient prolactin. The continuance of secretion of estrogenic hormone in cases of retained membranes amply explains the impairment of mammary function observed in this condition.

The clinical and postmortem observations in gynecomastia are variable and confusing. Aside from being found in true gynandromorphism, where it might be expected, it is also associated with tumors of the testis known to contain estrogenic substance, and with pituitary, adrenal and pineal tumors. It is very difficult as yet to evaluate degrees of gynecomastia in terms of estrogenic substance and prolactin, respectively. However, if the organism were saturated with estrogenic hormone and the anterior lobe did not secrete prolactin, no parenchymal growth over and above nipple and duct hypertrophy would occur. It is not unlikely that the presence of chorionepitheliomas with their high contents of estrogenic and gonadotropic hormones is inhibitory toward the prolactin secreting cells, since only about 6 per cent of these cases show gynecomastia.[40]

Since pituitary dysfunction rarely manifests itself with respect to a single hormone, it is not surprising that abnormal mammary hyperplasia with or without lactation has been found associated with gigantism or acromegaly in both sexes, indicating that at least two of the established anterior lobe hormones are in excess. Male impotence as well as amenorrhea, accompanied by abnormal breast development and lactation, may in some instances be due to hypogonadotropic hormone secretion coupled with oversecretion of prolactin, while lactation in sexually normal males with pituitary tumors implies hyperactivity of the prolactin secreting cells without impairment of the gonadotropic hormone secretion.

Until the physiopathologist duplicates the various abnormal breast hyperplasias with hormones in such a form as the hypophysectomized monkey, it would be better to abstain from too much conjecture regarding hormonic etiology. Animal experiments suggest, however, that abnormal nipple or duct growth may be accomplished by excess of estrogenic hormone alone, whereas abnormal alveolar hyperplasia may require preliminary stimulation by estrogenic substance followed by prolactin. By injecting estrogenic substance to inhibit prolactin secretion, Mazer[41] obtained some measure of regression in cases diagnosed by the effect of treatment as lobular hyperplasias. Geschickter and his colleagues[42] have partly reproduced the picture of fibro-adenoma in the male monkey by injections of estrogenic substance and prolactin.

One is tempted to search for hormonic explanations of the well known fact that the great bulk of benign mammary tumors occur before, while most malignant growths occur after, the menopause. Transplantable or spontaneous mammary tumors are partly inhibited in their growth by hypophysectomy and are accelerated by pituitary injections.[43] The slightest indication of a relationship between prolactin and the incidence or proliferation of malignant conditions will undoubtedly restrain the zeal of those clinicians anxious to improve breast function.

For a better understanding of abnormal breast conditions, a suitable test for prolactin in the body fluids is needed. With simultaneous assays of estrogenic and gonadotropic hormones and prolactin in bloods and urines, the gynecologist should be able more accurately to decide on the hormonic relationships in any given mammary condition, and the actual need of nursing mothers for prolactin therapy.[44]

IV. THYROTROPIC HORMONE

The discovery of thyroid-stimulating effects from anterior pituitary substance was made simultaneously and independently by Loeb and by Aron in 1929. It is now known that these thyreotropic[45] or thyrotropic effects are due to a specific hormone of the anterior lobe; i. e., to a substance which, although not yet finally purified, does not give the other effects of anterior lobe implants or extracts (somatotropic, gonadotropic and the like). As will be disclosed in a special paper of this series, its first approximate purification was achieved independently by Junckmann and Schoeller and by Loeser in 1932. The researches of the Aron group at Strasbourg, of Jansen and Loeser and their co-workers at Freiburg, and of Collip, Anderson and their associates at Montreal have done much to elucidate the biologic effects of this substance. The thyrotropic hormone exerts its action only in the presence of the thyroid gland, a complete thyroidectomy obliterating any and all of its specific effects.

Underproduction of Thyrotropic Hormone.—Pituitary ablation is invariably followed by hypothyroidism; conditions of underfunction of the pituitary could therefore be followed by hypothyroid states. One may therefore justifiably ask to what extent cretinism or myxedema may be regarded as being primarily pituitary and only secondarily thyroid disorders; i. e., due to inadequate amounts of thyrotropic hormone. Unfortunately the titration of the body fluids for thyrotropic

36. Nelson, W. O.: Reciprocal Relationship Between the Ovaries and Anterior Hypophysis as a Factor in Control of Lactation, Proc. Soc. Exper. Biol. & Med. **30**: 953 (April) 1933.
37. Pencharz, R. L. and Long, J. A.: Hypophysectomy in the Pregnant Rat, Am. J. Anat. **52**: 117 (July) 1933. Selye, Hans; Collip, J. B., and Thomson, D. L.: Effect of Hypophysectomy upon Pregnancy and Lactation, Proc. Soc. Exper. Biol. & Med. **30**: 589 (Feb.) 1933.
38. Corner, G. W.: The Hormonal Control of Lactation, Am. J. Physiol. **95**: 43 (Oct.) 1930.
39. Nelson, W. O.: Studies on the Physiology of Lactation, Endocrinology **18**: 33 (Jan.-Feb.) 1934.
40. Kriss, B.: Einige Bemerkungen zur Arbeit von Heidrich, Fels, und Mathias: Testiculares Chorionepitheliom mit Gynäkomastie, Arch. f. Gynäk. **145**: 327, 1931.
41. Mazer, C.: The Endocrine Glands in Relation to Abnormal Breast Hyperplasias, M. Rec. **140**: 417 (Oct. 17), 476 (Nov. 7) 1934.
42. Geschickter, C. F.; Lewis, Dean, and Hartman, C. G.: Tumors of the Breast Related to the Oestrin Hormone, Am. J. Cancer **21**: 828 (Aug.) 1934.
43. Further work of this nature might well take advantage of spontaneous, metastasizing, mammary tumors of mice, and a purified prolactin.
44. Kurzrok, R.; Bates, R. W.; Riddle, Oscar, and Miller, E. G.: The Clinical Use of Prolactin, Endocrinology **18**: 18 (Jan.-Feb.) 1934.
45. The term was first suggested by Wiesner and Crew.

hormone is not in as satisfactory a state as that concerning the gonadotropic hormones. It must be confessed that although Aron [46] and his associates feel that this titration can be effected and that the body fluids are indeed enormously high in thyrotropic hormone in myxedema,[47] his results are under dispute; Marie Krogh [48] denies their validity entirely. Paal [49] and Nielsen [50] both report the hormone in the urine. Giedosz,[51] while finding it in the urine, finds it in a motley array of disorders not specifically related to thyroid or pituitary disorders.

Overproduction of the Thyrotropic Hormone.—It has already been noted that Aron feels that one can recognize very high titers of this substance in many cases of myxedema, and it is interesting that the same observer reports his lowest recorded titers (subnormal amounts) in cases of exophthalmic goiter, which he is hence inclined to classify as primary thyroid overactivity not induced by overabundant thyrotropic substance.[52]

The discovery of an antithyrotropic hormone by Anderson and Collip, and the extension of this discovery to the detection of other anterior pituitary antihormones (antigrowth, antigonadotropic, antiketogenic) has introduced a new epoch of theoretical as well as clinical research. The amelioration of exophthalmic goiter by antithyrotropic hormone has already been reported, it being fortunate that the thyroid secretion does not oppose or modify the effects of antithyrotropic hormone. Collip's [53] conception that all hormones are accompanied by and "buffered" by a normal blood content of antihormone, and his statements that the antihormones do not arise concurrently with other known antibodies, all indicate that the phenomena are distinct from those hitherto studied in the field of immunity.

V. INTERRENOTROPIC HORMONE

There is both experimental and clinical evidence to support the concept of an interrelationship between the anterior pituitary and the cortical tissue of the adrenal gland. Houssay [54] and Shumacker and Firor [55] have both recently and rather comprehensively reviewed this subject.

Hypopituitary States.—Following hypophysectomy there is a rapid and extensive atrophy of the adrenal cortex, which can be restored by the use of pituitary implants or injections of extracts but not by injecting cortical hormone. It seems certain that this repair is due to a special hormone of the anterior lobe, the adrenotropic or, better, adrenocorticotropic or interrenotropic hormone.[56] Following unilateral adrenalectomy in normal animals there is a marked compensatory hypertrophy of the remaining adrenal, which does not take place in a hypophysectomized animal. In clinical conditions such as pituitary cachexia and dwarfism the adrenals have been reported as disproportionately small. In anencephaly the hypophysis is small or absent, and it is interesting that there is also hypoplasia of the adrenal cortex.

Hypocortical States.—Adrenalectomized rats can be made to grow by adequate treatment with cortical hormone, but this is not the case if the animal has been hypophysectomized. In Addison's disease, histologic changes occur in the pituitary gland, chiefly a diminution in the number of basophils. Similar changes have been found in the pituitary of an adrenalectomized dog. The treatment of Addison's disease with pituitary extract has been reported by Wilder.[57]

Hyperpituitary States.—The implantation of anterior pituitary tissue or injection of pituitary extracts into normal animals brings about a marked hypertrophy of the adrenals. This is apparently due to the same hormone that repairs adrenal-cortical atrophy after hypophysectomy, and the preparation of the hormone in a rather pure state has been reported.[58] The thyroid is necessary in this pituitary production of adrenal hyperplasia, although the thyrotropic hormone does not seem to be the essential cause of it, for pituitary extracts devoid of thyrotropic effects are able to produce the adrenal enlargement, and the enlargement cannot be produced by administering the thyroid hormone.[59] In cases of acromegaly, adrenal hyperplasia and cortical adenomas are often present, and one case has been reported in which an acromegalic girl suddenly developed hirsutism, interpreted as an adrenal effect.

Hypercortical States.—In addition to being essential for life, the adrenal cortex seems definitely related to the reproductive and integumentary system, as is well illustrated in a rather well defined group of changes produced by certain cortical tumors (interrenalism).[60] It remained for the acumen of Harvey Cushing to discover that a group of these cases is produced by basophilic adenoma of the pituitary (Cushing's disease).[61] Similar pictures are given by arrhenoblastomas

46. Aron, M.: Le titrage des hormones préhypophysaire dans l'urine humaine: son intérêt dans l'exploration functionelle des diverses glandes endocrines, Bull. Acad. de méd. Paris **111**: 273 (Feb. 20) 1934.

47. Aron's observations, if substantiated, will prove that many, if not most, cretinic and myxedematous conditions are primary thyroid disorders, just as the overabundance of gonadotropic hormone in the menopause and the primary amenorrheas indicate primary inability of the ovary to respond to gonadotropic hormones that are normally or even excessively present. Aron's results also explain the unfavorable results in the few cases in which thyrotropic therapy has been tried in myxedema. Schittenhelm and Eisler have for instance injected from 600 to 1,000 guinea-pig units daily of the thyrotropic hormone without significant improvement.

48. Krogh, Marie, and Okkels, H.: L'hormone thyréo-stimulante de la préhypophyse, Compt. rend. Soc. de biol. **116**: 255 (April 12) 1934.

49. Paal, H.: Ueber Hormothyrin, das Schilddrüsenanregende Hormon des Hypophysenvorderlappens, Klin. Wchnschr. **10**: 2172 (Nov. 21) 1931.

50. Nielsen, Herman: Ein "Thyreotest" durch Harninjektion in Kaninchen, Klin. Wchnschr. **12**: 508 (April 1) 1933.

51. Giedosz, B.: Ueber thyreotrope Substanzen im menschlichen Harn, Klin. Wchnschr. **13**: 1507 (Oct. 20) 1934.

52. It may be felt that such a deduction can hardly be allowed conclusive validity, for it is conceivable that a hypertrophied thyroid could demand and utilize such large amounts of the thyrotropic hormone as to depress the normal titer in this substance. On the other hand, Aron and others have shown that thyroxine renders thyrotropic hormone inefficacious and thyroid overactivity might therefore automatically control itself in the normal mechanism, quite apart from the thyrotropic-antithyrotropic balance. The improvement in some cases of exophthalmic goiter following roentgen therapy of the pituitary, reported by Merklin and Aron (1933) and by Peters (1934), lends inadequate support to the conception of pituitary exophthalmic goiter.

53. Collip, J. B.: Inhibitory Hormones and the Principle of Inverse Response, Ann. Int. Med. **8**: 10 (July) 1934.

54. Houssay, B. A.: Relaciones entre la hipofisis y las suprarrénales, Prensa méd. argent. **20**: 1563 (July 19) 1933.

55. Shumacker, H. B., and Firor, W. M.: The Interrelationship of the Adrenal Cortex and the Anterior Lobe of the Hypophysis, Endocrinology **18**: 676 (Nov.-Dec.) 1934.

56. If the carbohydrate upset caused by the anterior lobe extracts should be established as an epinephrine diabetes (hyperepinephrinism) thus produced by a pituitary hormone, it may then be appropriate to speak of the latter as the adrenomedullotropic or chromaffinotropic hormone.

57. Wilder, R. M.: The Use of Anterior Lobe Pituitary Extract in the Treatment of Addison's Disease, Proc. Staff Meet., Mayo Clin. **9**: 689 (Nov.) 1934.

58. Collip, J. B.; Anderson, E. M., and Thomson, D. L.: The Adrenotropic Hormone of the Anterior Pituitary Lobe, Lancet **2**: 347 (Aug. 12) 1933. Anselmino, K. J.; Hoffman, F., and Herold, L.: Ueber das corticotrope Hormon des Hypophysenvorderlappens, Klin. Wchnschr. **13**: 209 (Feb. 10) 1934.

59. McQueen-Williams, M.: Necessary Concurrence of the Thyroid in the Marked Adrenal Cortical Hypertrophy Following Beef Anterior Pituitary Implants, Proc. Soc. Exper. Biol. & Med. **29**: 296 (Nov.) 1934. Emery, F. E., and Winter, C. A.: The Adrenotropic Substance of the Hypophysis as Influenced by Age, Castration, Sex and Thyroparathyroidectomy, Anat. Rec. **60**: 381 (Nov.) 1934. Loeser, A.: Beziehungen zwischen der thyreotropen Substanz des Hypophysenvorderlappens und den Nebennieren, Klin. Wchnschr. **13**: 1614 (Oct. 14) 1933.

60. Walters, Waltman; Wilder, R. M., and Kepler, E. J.: Suprarenal Cortical Syndromes, Ann. Surg. **100**: 670 (Oct.) 1934.

61. Cushing, Harvey: The Basophil Adenomas of the Pituitary Body and Their Clinical Manifestations, Bull. Johns Hopkins Hosp. **50**: 137 (March) 1932.

of the ovaries.[61a] The many symptoms common to these groups form strong substantiation for a special pituitary-adrenal-gonadal interrelationship. The titration of the body fluids for the gonadal and gonadotropic hormones in these various conditions has not yet been adequately undertaken.[62] Pituitary transplants have been found to have an effect on the reproductive system of adrenalectomized animals, but cortical hormone did not affect hypophysectomized animals.

VI. METABOLIC HORMONES

In addition to the metabolic effects that have already been mentioned in the discussion of the thyrotropic and interrenotropic hormones, there have been studies made on some special relationships of the anterior hypophysis to metabolism. These deal largely with the metabolism of carbohydrate and fat, and to a less extent of protein. The interpretation of such studies is especially difficult because of the many species used, the varying technics of operation, the many types of extracts injected, the different methods of chemical analysis, and the acknowledged interrelationship of many factors other than the pituitary gland involved in general metabolism.

Until recently it seemed most likely that water metabolism was controlled solely by hypothalamic centers to which it was admitted the posterior lobe had a relation not wholly understood, the outstanding fact being the therapeutic control of diabetes insipidus with posterior lobe extracts. Evidence of a relation of the anterior lobe to water metabolism has recently been furnished. I shall not discuss this but concern myself with the more carefully investigated but perhaps equally obscure relation of the anterior lobe to carbohydrate, fat and protein metabolism.

Carbohydrate Metabolism.—This field may be considered as having been opened by the announcement of Houssay and Magenta in 1924 that hypophysectomized dogs have a markedly increased sensitiveness to insulin. This has been confirmed abundantly, although it awaits thoroughgoing elucidation. In 1930 Biasotti and Houssay extended to mammals an experience with toads to the effect that hypophysectomy lessens the severity of diabetes from pancreatectomy and that after such double operations an intensification of the diabetes ensues from anterior lobe but not from posterior lobe implants. These announcements, sufficiently spectacular, suffered temporary neglect, but energetic refutation or confirmation and extension of the Houssay phenomena is now being undertaken. In 1932 came the independent announcements by Evans and his co-workers and by Houssay of the production of hyperglycemia and glycosuria in normal animals by injection of anterior pituitary extracts.

This, which is perhaps the most deeply interesting field of pituitary research, continues to remain in the least satisfactory state, and clinical applications are premature.

The studies that have been made on hypophysectomized animals may be summarized thus:

1. A temporary glycosuria occurs which, it is generally agreed, is secondary to cerebral trauma rather than to the absence of the gland.

2. Hypoglycemia develops sometimes to the point of convulsions and death.

3. The animals are markedly more sensitive to small amounts of insulin.

4. The intensity of the diabetes of pancreatectomized dogs is lessened.[63]

5. The glycogen reserves are usually reported as diminished, though some reports of their normality have been made.

As regards normal animals injected with pituitary extracts, one may state that:

1. Disturbed carbohydrate metabolism is manifest by glycosuria, hyperglycemia and decreased (diabetic) sugar tolerance curve.

2. Houssay reports that these effects can still be secured in the absence of various organs including the thyroids, adrenal medulla, gonads and sympathetic nerves. Lucke states that the adrenal is essential.

3. Most of the effects of the extracts require chronic injections for several days. Only Lucke reports effects within a few hours.

4. With the disturbance in carbohydrate metabolism there are associated disturbances in fat metabolism.

The new conception that diabetes may be due to an overacting hypophysis[64] and not solely to inadequate pancreatic insular function is engaging, but the only conclusion now warranted is that, while there is some substance in the anterior pituitary that affects carbohydrate metabolism, the isolation of a special "diabetogenic" or "contra-insular" hormone has not yet been effected.

Fat Metabolism.—Hoffman and Anselmino (1931) and Magistris (1932) have secured from the anterior pituitary of beeves a material causing increased acetonemia and simultaneous diminution of the neutral fats of the blood. Bevin and Ling (1933) found increased acetonuria of rats on a butter diet when injected with alkaline extracts of bovine anterior pituitary. Extracts containing the thyrotropic hormone had been reported to give some of these effects, so that it is important that Black, Collip and Thomson[65] have recently secured the increased acetonuria in thyroidectomized rats. The evidence adduced up to the present time makes it probable that the "ketogenic principle" is indeed a separate hormone, for, although it contaminates growth and thyrotropic fractions, it may be secured in growth fractions free of thyrotropic and in thyrotropic fractions free of growth hormone, and it is said to be absent from the best adrenotropic preparations.

Protein Metabolism.—O. H. Gaebler[65a] and Lee and Schaffer[66] have demonstrated the retention of nitrogen provoked by the growth hormone. Houssay and his associates report that in phlorhizinized, hypophysectomized dogs, sugar and nitrogen excretion is markedly less than in unoperated on or thyroidectomized animals

61a. Meyer, Robert: The Pathology of Some Special Ovarian Tumors and Their Relation to Sex Characteristics, Am. J. Obst. & Gynec. 22: 607 (Nov.) 1931.

62. Though in one instance a substance having the effects of the testis hormone was found in a woman's urine (Simpson, S. L.: Clinical and Pathological Aspects of the Adrenal Glands, Proc. Roy. Soc. Med. 27: 383, 1934).

63. Unfortunately, not all published reports contain detailed necropsies.

64. Some special students of the subject state that no pathognomonic lesions of the islets have ever really been established in diabetes mellitus. But the newer studies of E. J. Kraus, Labbé and Petresco, Glenn and others on the microscopic pathologic changes of the pituitaries of patients dead from diabetes are not more satisfactory. Barnes and his co-workers have sought to improve diabetes by injections of estrogenic substance which would depress pituitary function; diabetic treatment by radiation of the pituitary has been attempted with inconclusive results. Selle and his co-workers (Selle, W. A.; Westra, J. J., and Johnson, J. B.: Effect of Irradiation of the Hypophysis on Experimental Diabetes, Proc. Soc. Exper. Biol. & Med. 31: 949 [May] 1934) were unable to affect diabetes in dogs by roentgen therapy.

65. Black, P. T.; Collip, J. B., and Thomson, D. L.: The Effect of Anterior Pituitary Extracts on Acetone Body Excretion in the Rat, J. Physiol. 82: 385 (Oct. 17) 1934.

65a. Gaebler, O. H.: Some Effects of Anterior Pituitary Extracts on Nitrogen Metabolism, Water Balance and Energy Metabolism, J. Exper. Med. 57: 349 (March) 1933.

66. Lee, M. O., and Schaffer, N. K.: Anterior Pituitary Growth Hormone and the Composition of Growth, J. Nutrition 7: 337 (March 10) 1934.

given phlorhizin.[67] The former die in hypoglycemic crises whereas the latter do not. Death can be prevented by feeding meat or sugar but not by feeding fat. These observations are interpreted to mean that in the absence of the hypophysis there is an interference with the conversion of protein to carbohydrate.

Varying results have followed the studies of the specific dynamic action in hypophysectomized animals and in clinical cases of hypopituitary disease. No conclusions can be drawn from the work at this time.

Clinical studies are not yet able to yield critical information regarding the relationship of the pituitary to metabolism. Perhaps the earliest noted and best established phenomenon is the occurrence of glycosuria in about 40 per cent of the cases of acromegaly.

The possible rôle of the pituitary in spontaneous hypoglycemia has been raised by Josef Wilder, who reported two cases with roentgen evidence of enlargement of the sella. Were a contra-insular hormone available, it would be interesting to see its effect in those particular cases of this unfortunate condition in which no island tumor of the pancreas is found.

While there can be no doubt that the pituitary gland plays a rôle in the metabolism of carbohydrates, fats and probably proteins, its modus operandi will not be sufficiently clarified until the researches of the immediate future are accomplished. Its rôle may be to furnish specific hormones that act in conjunction with or as antagonists to other hormones. In many laboratories, efforts are being made to obtain these substances in at least partially purified form, though none are yet available for clinical use.

CONCLUSION

The reader must not carry away the impression that the foregoing discussion comprises all that is known of the relations of the anterior pituitary with other glands and tissues of the body. Indications of a special relation with the parathyroid are beginning to appear, and a rôle in erythropoiesis has been claimed. An insular-pancreotropic and an adrenomedullotropic hormone have been foreshadowed.

The study of the possible derangement of many physiologic mechanisms in hypophysectomized animals has hardly begun. Finally, this review has neglected completely the relation of the pituitary with the hypothalamus. Future discoveries may irrefutably establish humeroneural mechanisms concerning which almost nothing is now known.

It is perhaps somewhat surprising that not one of the five established pituitary hormones is accurately known chemically. The protein nature of these substances has undoubtedly played a chief rôle in their intractability. Yet in all cases a wide going purification has been attained, the minimal effective daily dose for test animals in the case of all them being below a milligram of substance.

The desirability of increasing our power to estimate these materials quantitatively in the blood stream or urine could hardly be overstressed, and in the case of each one of them one must covet for the internist of the future the satisfaction now possessed by the gynecologist in his ability to determine the titers of estrogenic and gonadotropic hormones in the body fluids.

67. Biasotti, A., and Houssay, B. A.: Phloridzin Diabetes in Fasting or Fed Hypophysectomized Dogs, J. Physiol. 77:81 (Dec.) 1932. Houssay, B. A.; Biasotti, A.; di Benedetto, E., and Rietti, C. T.: Actions des extrait antéro hypophysaire sur le diabète phlorhyzinique, Compt. rend. Soc. de biol. 112:497 (Feb. 10) 1933.

Therapeutics

THE THERAPY OF THE COOK COUNTY HOSPITAL

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CHICAGO

NOTE.—In their elaboration, these articles are submitted to the members of the attending staff of the Cook County Hospital by the director of therapeutics, Dr. Bernard Fantus. The views expressed by various members are incorporated in the final draft for publication. The series of articles will be continued from time to time in these columns.—ED.

THERAPY OF UNCINARIASIS

Uncinariasis should be thought of in any case of hypochromic anemia with eosinophilia, though the absence of eosinophilia does not eliminate uncinariasis, as in very severe cases the eosinophil count may fall to the normal average or even below it. A stool examination is called for, especially if there is also a history of exposure in infested regions. While the dried smear examination may show the eggs, it is best to stir up a gram of feces with about 20 cc. of saturated solution of sodium chloride. After about fifteen minutes, the eggs floating on the surface are transferred, possibly by means of the mouth of an inverted test tube, to the microscopic slide.

PROPHYLAXIS

The prophylaxis depends on proper disposal of the feces of all infected persons (sanitary latrines), avoidance of walking barefoot, and thorough treatment of all infested persons, which, if possible, would greatly hasten the eradication of the disease.

TREATMENT

The treatment of uncinariasis is a story in two chapters: the expulsion of the worms and the cure of the anemia.

PRESCRIPTION 1.—*Tetra-Chloro-Ethylene Capsules*

℞ Tetra-chloro-ethylene ..... 3.00 cc.
Divide into six capsules.
Label: Take in the morning on empty stomach.

1. *Anthelmintic.*—Tetra-chloro-ethylene is the preferred agent at present. It requires no preliminary measures, excepting that the patient have no breakfast. Instead of this meal the patient takes 3 cc. of tetra-chloro-ethylene, preferably in capsules (prescription 1), followed immediately by a dose of 30 Gm. of magnesium sulphate dissolved in a glassful of water. If the patient believes he cannot swallow capsules, the tetra-chloro-ethylene is poured on a little sugar and is thus taken readily. Children are given 0.2 cc. for each year of age and 2 Gm. of magnesium sulphate for each 5 Kg. of body weight. The patient should rest until the purge has acted; if it does not act within a few hours, a second dose of purgative should be taken. After the bowel evacuation, the patient may eat, preferably cooked cereal. It is probably well to avoid the use of fats or alcohol just before and after administration of the drug, as these favor its absorption. Its chief untoward effect is the occasional production of a transient dizziness, sometimes nausea, vomiting, headache, abdominal pains and malaise. The patient should be warned against their possible occurrence. They usually do not require treatment.

After two weeks a stool examination should be made, and if no ova are found in flotation preparations the worms may be considered eradicated. If they are found, the treatment should be repeated, possibly with a dose of 4 cc. of tetra-chloro-ethylene.

PRESCRIPTION 2.—*Reduced Iron Capsules*

℞ Reduced iron..... 30.00 Gm.
Divide into thirty capsules.
Label: Take two capsules three times daily after meals.

2. *Hematinic.*—While there is a tendency to blood regeneration after expulsion of the worms, iron decidedly hastens this recovery, if given in large doses (e. g., as in prescription 2).

3. *General Regimen.*—Usually the patient may be permitted to continue with his occupation. Bed treatment is required only in extreme cases, especially in those with edema. An abundance of nutritious food is required in addition to the iron to favor rebuilding of the much depleted blood; and, no doubt, fresh air and sunshine are also useful in this direction.

THERAPY OF TRICHINIASIS

DIAGNOSIS

Marked eosinophilia should always lead one to suspect the possibility of some form of helminthiasis, though it must be remembered that eosinophilia may be due to many other conditions and that it is especially common in children. Some of the manifestations of the classic syndrome muscle pain, edema and fever might then suggest trichiniasis, the presence of which is rendered probable by discovery of the cysts in the suspected pork, and proved by the finding of the worms in the feces (difficult), in muscle tissue (after surgical excision under local anesthesia of a piece of the biceps, deltoid or gastrocnemius), or in the spinal fluid (after centrifugation) in cases presenting meningeal symptoms. The presence or absence of the trichiniasis skin test[1] strengthens the evidence for or against this diagnosis.

PROPHYLAXIS

Unfortunately, the usual microscopic inspection of fresh pork and pork products is no adequate criterion of freedom of the pork from trichinae. As complete cooking of pork will absolutely prevent the disease, every one should be educated to the importance of eating only thoroughly cooked pork and pork products. "Cook pork well" is the slogan of prevention; and it must be remembered that an adequate degree of heat (137 F.) is slow in reaching the center of a thick piece of meat. Refrigeration kills the encysted larvae, but it must be at 0 F. for forty-eight hours.

TREATMENT

1. *Active Purgation.*—Even in cases not seen until six weeks after infection, active purgation should not be neglected. Mild Mercurous Chloride, in doses of 0.2 Gm., followed in six or eight hours by Magnesium Sulphate (30 Gm.) and this by a colon flushing several hours later, might be repeated for several days, in the hope of sweeping out some of the worms that have not yet invaded the submucosa.

2. *General Care.*—In cases presenting fever, it is fever regimen (q. v.) followed during convalescence by a long period of rest and highly nutritive diet.

1. McCoy, O. R.; Miller, J. J., Jr., and Friedlander, R. D.: The Use of the Intradermal Test in the Diagnosis of Trichiniasis, J. Immunol. 24:1 (Jan.) 1933.

3. *Relief of Clinical Manifestations.*—(*a*) Myositis: Muscular pain, when well localized, might be relieved by limitation of motion by means of adhesive plaster strapping, provided it is not applied tightly enough to aggravate the muscular soreness. Morphine might be required, if milder analgesics fail (cf. Therapy of Pain). It has been suggested that treatment with Calcium, as in the accompanying prescription, and parathyroid extract (from 20 to 40 units every twelve hours for not more than ten days) might hasten calcification of the cysts and thus shorten the course of the trichinal "rheumatism."

Calcium Lactate

℞ Calcium lactate..... 20.00 Gm.
Lactose..... 40.00 Gm.
Dispense in a box.
Label: Heaping teaspoonful in water before meals and at bedtime.

(*b*) Allergic Symptoms: Urticaria, pruritus and the late edema, appearing about three weeks after the ingestion of the parasites, might possibly be benefited by Solution of Epinephrine (from 0.5 to 1 cc.) injected intramuscularly and repeated as often as the rather transient improvement might demand.

(*c*) Meningismus: This might be ameliorated by lumbar puncture.

(*d*) Failure of Respirations: The failure of respirations from muscular involvement might call for treatment in a respirator.

DISCUSSION OF PREVIOUSLY PUBLISHED ARTICLES

DISTURBANCES DUE TO HEAT

To the Editor:—May I submit the following comment on the article on the therapy of disturbances due to heat (THE JOURNAL, September 29, p. 990):

Recent experience has fairly demonstrated that heat exhaustion is essentially dehydration. The human body is dependent on the vaporization of water from its surface for the dissipation of excessive heat. Water passing from a liquid to a vapor requires heat. This it takes from the body, thereby cooling it. Hence the call for water and more water, perspiration and more perspiration, depletion of water, dehydration and shock. There is no injury to the machinery of the body. All it needs is volume of water, and salt to maintain the proper osmotic balance. This dehydration precedes by considerable time any damage from hyperpyrexia. To still advise bleeding for sunstroke seems a bit out of date. The unconsciousness is due to brain anemia, and the demand is for fluid to fill the blood vessels and thus restore the needed pressure in the brain.

It is realized by all that by perspiration 8 or 10 pounds up to 20 pounds can be lost in one day. Most football players lose 6 or 8 pounds for each game, and still the coaches insist that they must not drink during the game.

The experiences at Hoover Dam, at the Los Angeles aqueduct and at numerous other places in California and elsewhere demonstrate this principle. At these points the prophylaxis is the same as that advised by Dr. Fantus and he has covered it very well. If he had simply continued the same fundamental principle into his therapeutics he would save many lives and many days of illness, because it has been repeatedly demonstrated that intravenous salt or dextrose solution will by filling the empty blood vessels almost immediately put patients on their feet.

Pathologists find the heart and major blood vessels empty at autopsy and the skin suffused with what little blood is left in the body. This dusky cyanotic picture has always suggested bleeding, and this undoubtedly is the basis of the advice in this article to draw blood in the asphyxial form of heat exhaustion.

However, the mechanics of the condition indicates that instead of depletion there is a demand for fluid to fill the central blood vessels. The essential mechanics is that heat dilates capillaries and increases the permeability and keeps on dilating them and drawing blood from the heart and large blood vessels until cyanosis appears. The capillary permeability sometimes is so great that ecchymoses result.

The records at Hoover Dam are striking and are summarized as follows:

Summer of 1931: From 100 to 150 cases (no record); 17 deaths.

Summer of 1932: Seven cases; no deaths. (Prevention and treatment based on the dehydration principle were instituted in the spring of 1932.)

Summer of 1933: Thirteen cases; no deaths.

Summer of 1934: Very few cases; no record; no deaths.

A record of these experiences is given by Dr. R. O. Schofield, "Heat Prostration—Its Treatment at Boulder Dam," in *California and Western Medicine* **41**:83 (Aug.) 1934.

Further references are:

Van Zwalenburg, Cornelius: Heat Prostration and Dehydration, THE JOURNAL, Oct. 17, 1931, p. 1169.

Dehydration in Heat Exhaustion and in Fatigue, *California & West. Med.* **38**: 354 (May) 1933.

Heat Prostration and Dehydration, THE JOURNAL, Oct. 14, 1933, p. 1253.

Prevention and Treatment of Heat Exhaustion and Sunstroke, *Weekly Bulletin, California State Department of Public Health* **13**, June 16, 1934.

Dill, D. B.; Bock, A. V., and Edwards, H. T.: Mechanisms for Dissipating Heat in Man and Dog, *Am. J. Physiol.* **104**: 36 (April) 1933.

CORNELIUS VAN ZWALENBURG, M.D., Riverside, Calif.

COMMENT.—Unfortunately, the pathology of an established case of sunstroke is not simple dehydration, as is shown by the fact that mere rehydration is usually not sufficient for cure. Even though dehydration might have been the original factor, secondary changes are present in sunstroke, as is evidenced, for instance, by the postmortem changes, among which multiple hemorrhages are quite common. Bleeding, of course, is not advocated and should not be resorted to until after thorough and complete rehydration. It is only then, and especially if symptoms of increased intracranial tension or of pulmonary edema manifest themselves, that bleeding might be thought of.

THERAPY OF CARBUNCLE

Dr. Sumner L. Koch presents the following much simpler treatment for carbuncle than that described in THE JOURNAL, Oct. 6, 1934, page 1066:

It is my belief that carbuncles, particularly small carbuncles, should be treated in the early stages by the application of warm wet dressings. If spread of inflammation is not halted and drainage does not take place promptly, the infected area should be opened; but the operative treatment should be confined to incision, undercutting of the flaps and the insertion of soft drainage material, such as petrolatum gauze or rubber tissue, simply to keep the flaps from falling back in place and immediately becoming adherent again to the surface from which they had become separated. Surgical treatment should be followed by the continued application of warm wet dressings until the acute inflammation subsides. When the acute inflammatory process has subsided, the use of dressings saturated with surgical solution of chlorinated soda undoubtedly is helpful in dissolving the necrotic tissue and so taking away the most important part of the culture medium for the bacteria present.

Until we can impress our students with the fact that tissues, whether normal or infected, are delicate living structures that need to be handled with every possible care and protected from every possible insult and injury, we shall fail in our purpose. The sooner we can get rid of the old idea that phenol, iodoform gauze, pastes and salves are helpful in the treatment of an infectious process associated with sloughing and necrosis of tissue, the better off we shall be.

COMMENT.—*Simplex est sigillum veri* (the simple is the sign of the truth) is probably correct in medicine as well as in philosophy.

RINGWORM OF THE HAIRY PARTS

To the Editor:—Referring to the article on the treatment of trichophytosis (The Therapy of the Cook County Hospital) appearing in THE JOURNAL, Sept. 15, 1934, page 832, attention should be directed to the paragraph headed "Ringworm of the Hairy Parts." The treatment there recommended consists of temporary epilation by means of roentgen rays, thallium or manual extraction. Epilation therapy is requisite in only certain forms of trichophytosis capitis—chiefly that caused by Microsporon Audouini. In many cases of ringworm of the scalp, the causative fungus is an "animal-borne" fungus, producing inflammatory and kerionic scalp lesions in children; these do not require depilation, as the large majority of them are readily curable by means of local antiseptic ointments.

Recently this fact was brought to the attention of readers of the Year Book of Dermatology and Syphilology (Year Book Publishers, Chicago) for 1933, page 267, by its editors, in a comment following an article on ringworm by R. L. Gilman. A more detailed discussion will be found in an article by George M. Lewis: Ringworm of the Scalp: A Report of Three Cases Due to the Microsporon Lanosum with a Tendency to Spontaneous Recovery, *Arch. Dermat. & Syph.* **29**:890 (June) 1934.

FRED WISE, M.D., New York.

Committee on Foods

ACCEPTED FOODS

THE FOLLOWING PRODUCTS HAVE BEEN ACCEPTED BY THE COMMITTEE ON FOODS OF THE AMERICAN MEDICAL ASSOCIATION FOLLOWING ANY NECESSARY CORRECTIONS OF THE LABELS AND ADVERTISING TO CONFORM TO THE RULES AND REGULATIONS. THESE PRODUCTS ARE APPROVED FOR ADVERTISING IN THE PUBLICATIONS OF THE AMERICAN MEDICAL ASSOCIATION, AND FOR GENERAL PROMULGATION TO THE PUBLIC. THEY WILL BE INCLUDED IN THE BOOK OF ACCEPTED FOODS TO BE PUBLISHED BY THE AMERICAN MEDICAL ASSOCIATION.

RAYMOND HERTWIG, Secretary.

KELLOGG'S ALL-BRAN

FLAVORED WITH MALT, SUGAR AND SALT

Manufacturer.—Kellogg Company, Inc., Battle Creek, Mich.

Description.—Cooked wheat bran flavored with sucrose, malt extract and salt.

Manufacture.—Wheat bran is cooked under steam pressure with water, sucrose, malt syrup and sodium chloride. The mixture is partially dried, shredded, toasted, cooled and packed in wax paper lined cartons.

Analysis (submitted by manufacturer).—

	per cent
Moisture	2.3
Ash	8.2
Sodium chloride	3.1
Fat (ether extraction method)	3.2
Protein (N × 5.7)	12.7
Reducing sugars as maltose	2.6
Sucrose	9.0
Crude fiber	7.7
Carbohydrates other than crude fiber (by difference)	45.9
Calcium (Ca)	0.10
Phosphorus (P)	1.34
*Iron (Fe)	0.017
†Copper (Cu)	0.0010

* J. Biol. Chem. **90**: 463 (April) 1930.
† J. Biol. Chem. **81**: 435 (Feb.) 1929.

Calories.—3.4 per gram; 97 per ounce.

Vitamins.—One ounce furnishes 45 Sherman and Chase vitamin B units.

Claims of Manufacturer.—Bran fiber is more resistant to disintegration in the intestine than is the fiber of fruit or vegetables and is therefore more effective for counteracting constipation due to insufficient bulk. Good source of vitamin B and iron.

GIRAFFE VACUUM PACKED FLORIDA NATURAL ORANGE JUICE

Manufacturer.—Tropical Juice Corporation of Florida; Miami and Titusville, Fla.

Description.—Canned orange juice; no added sugar or flavoring; retains in high degree the natural vitamin content.

Manufacture.—Tree ripened Florida oranges are washed, disinfected with borax or soda ash, rinsed, and stored in clean bins until used. The fruit is automatically halved. The juice is burred out by machine, the pressure being adjusted to avoid as far as possible extracting essential oil from the peel. The juice is strained through a series of screens, cooled to 4 C., processed at mild temperature, filled into containers which are sealed under reduced pressure (15 inches), processed at 71 C. for fifteen minutes, and cooled.

Analysis (submitted by manufacturer).—

	per cent
Moisture	87.0
Total solids	13.0
Ash	0.5
Fat (ether extract)	0.0
Protein (N × 6.25)	0.8
Reducing sugar as invert sugar	4.5
Sucrose	5.3
Crude fiber	0.0
Carbohydrates (by difference)	10.9
Titrable acidity as citric acid	0.8
Test for borax	negative

Calories.—0.5 per gram; 14 per ounce.

Vitamins.—Assay shows retention in high degree of vitamin C content.

Claims of Manufacturer.—Retains practically all the nutritive values of orange juice. For all dietary and table uses.

VITAMIN D FORTIFIED HOMOGENIZED PASTEURIZED MILK

Distributors.—Babcock's Diary Company, Port Huron, Mich. Alfar Creamery Company, West Palm Beach, Fla.

Description.—Bottled homogenized pasteurized milk fortified with vitamin D (vitamin D concentrate extracted from cod liver oil); contains 400 U. S. P. X (Revised, 1934) vitamin D units per quart.

Preparation.—The milk complies with legal requirements and is homogenized and pasteurized by the standard holding method. See THE JOURNAL, July 1, 1933, page 34, for description of fortification with vitamin D.

Vitamins.—The vitamin D concentrate used and the fortified milk are regularly tested biologically. Clinical investigation shows this milk to be a reliable antirachitic agent if the proper amount is used.

Claims of Distributors.—A vitamin D fortified, antirachitic homogenized pasteurized milk having otherwise the flavor and food values of usual homogenized pasteurized milk. The cream does not separate.

AMERICAN LADY BRAND STRAINED BEETS, CARROTS, CELERY, GREEN BEANS, PEAS, PRUNES FLAVORED WITH LEMON JUICE, SPINACH, TOMATOES, AND VEGETABLES WITH CEREAL AND BEEF BROTH

UNSEASONED

Distributor.—General Grocer Company, St. Louis.

Packer.—The Larsen Company, Green Bay, Wis.

Description.—Respectively sieved beets, carrots, celery, green beans, peas, prunes flavored with lemon juice, spinach, tomatoes and vegetables (carrots, potatoes, tomatoes, celery, peas, beans, spinach) with pearl barley and beef extract; prepared by efficient methods for retention in high degree of the natural mineral and vitamin values. No added sugar or salt. These products are the same as the respective accepted Larsen's vegetables and fruits (THE JOURNAL, July 1, 1933, p. 35; July 8, 1933, p. 125; July 22, 1933, p. 282; July 29, 1933, p. 366; Aug. 12, 1933, p. 525; Aug. 19, 1933, p. 605; Aug. 26, 1933, p. 675; Sept. 2, 1933, p. 779).

DAVIDSON'S ANGEL FOOD CAKE

Manufacturer.—Davidson Baking Company, Portland, Ore.

Description.—Angel food cake prepared from egg whites, sucrose, flour, cream of tartar, vanilla extract, sodium chloride and baking powder.

Manufacture.—The formula ingredients are worked into the egg whites in definite order. The batter is scaled, baked and cooled and the cake packed in cartons.

Analysis (submitted by manufacturer).—

	per cent
Moisture	29.8
Ash	0.7
Fat (ether extraction method)	0.2
Protein (N × 6.25)	7.1
Reducing sugars as dextrose	0.7
Sucrose	48.3
Crude fiber	0.03
Carbohydrates (by difference)	62.2
Lipoid phosphoric acid (P_2O_5)	0.01

Calories.—2.8 per gram; 80 per ounce.

Claims of Manufacturer.—White of thirteen eggs contained in each cake (1½ pounds).

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1. CHAPIN BRAND TOMATO JUICE
2. ECCO TOMATO JUICE
3. FFOG BRAND TOMATO JUICE
4. FI-NA-ST PURE TOMATO JUICE
5. GARDEN BRAND TOMATO JUICE
6. GIBRALTAR TOMATO JUICE
7. ISLAND CLUB SPECIAL TOMATO JUICE
8. MATCHLESS BRAND TOMATO JUICE
9. RADIO TOMATO JUICE

Distributors. — 1. Chapin Grocery Specialties Co., Inc., Springfield, Mass. 2. Economy Grocery Stores Corp., Boston. 3. Ridenour-Baker Grocery Company, Kansas City, Mo. 4. First National Stores, Inc., Somerville, Mass. 5. John Price & Company, Philadelphia. 6. H. L. Caplan & Co., Inc., Baltimore. 7. Lawrence Grocery Corp., Lawrence, Mass. 8. Webster-Thomas Company, Boston. 9. M. J. Caplan & Co., Inc., Lawrence, Mass.

Packer.—Vincennes Packing Corporation, Vincennes, Ind.

Description.—Pasteurized tomato juice with added salt; retains in high degree the natural vitamin content. The same as Alice of Old Vincennes Tomato Juice (THE JOURNAL, Feb. 20, 1932, p. 640).

PERFECTION FLOUR (BLEACHED)

Manufacturer.—The Robinson Milling Company, Salina, Kan.

Description.—Hard winter wheat straight flour; bleached.

Manufacture.—Selected hard winter wheat is cleaned, scoured, tempered and milled by essentially the same procedures as described in THE JOURNAL, June 18, 1932, page 2210. Chosen flour streams are blended and bleached with a mixture of benzoyl peroxide and calcium phosphate (14.2 Gm. per barrel) and nitrogen trichloride (4 Gm. per barrel).

Analysis (submitted by manufacturer).—

	per cent
Moisture	13.0
Ash	0.4
Fat (ether extraction method)	1.2
Protein (N × 5.7)	10.6
Starch	69.5
Crude fiber	0.4
Carbohydrates other than crude fiber (by difference)	72.4

Calories.—3.4 per gram; 97 per ounce.

PENFORD BRAND GOLDEN SYRUP
PENFORD BRAND CRYSTAL WHITE SYRUP

Manufacturer.—Penick and Ford Sales Company, Inc., Cedar Rapids, Iowa.

Description.—Table syrups; corn syrup flavored with refiners' syrup and corn syrup sweetened with sucrose; the same as the accepted Penick Golden Syrup (THE JOURNAL, April 2, 1932, p. 1159) and Penick Crystal White Syrup (THE JOURNAL, April 9, 1932, p. 1268) respectively.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

535 North Dearborn Street - - - Chicago, Ill.

Cable Address - - - - "Medic, Chicago"

Subscription price - - - - - Seven dollars per annum in advance

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SATURDAY, FEBRUARY 9, 1935

PSYCHOLOGIC CONCOMITANTS OF PAIN

Pain in its various aspects offers an attractive field for study and speculation. According to Waterston [1] it is often, but not invariably, accompanied by other symptoms, such as pallor, fainting and sweating; these are sometimes ascribed to the pain. They are not, however, invariable concomitants of pain and may hence be produced in a different way, by afferent impulses other than those which cause pain, traveling by a different path and producing their effects often by exciting the sympathetic system.

The psychologic concomitants of pain, Critchley [2] says, are manifold. An acute and severe pain usually dominates the victim's sensorium, often to the exclusion of other internal and external impressions. Inability to concentrate and irritability are of frequent occurrence during states of painful experience. The major affects of rage, fear, anxiety or despair may also accompany the feeling of pain. Their presence depends on the nature of the pain and the circumstances surrounding its production. Under the stress of an agonizing experience the sense of time may be disordered. This effect is commonly expressed as "each minute seemed an hour." Mental depression is, however, rare as a concomitant of severe pain. Thus, as Ribot puts it, "It seems as though the organism had but a limited capacity for either pleasure or pain, and that neither feeling can exist at the same time in its double (physical and moral) form." Sleep may follow intense suffering, and in that which succeeds or accompanies the exhaustion of torture, dreams of a peculiarly vivid or complex character are often experienced. Jack London has described in The Jacket (the Star Rover) the particularly coherent and continuous visions of Durrell Standing while undergoing a series of ordeals by strait-jacket: "He would dream that he was addressing learned societies on abstruse problems, often waking to the sound of his voice ringing in his ears and with imaginary pages of manuscript floating before his eyes; that he was journeying on horseback through the meadows of some vast farm; day by day the dream story would develop coherently and consecutively, and unroll itself before him. Shrubs and plants would grow from small beginnings into tall vegetation, which would later be felled by the laborers' axes, collected, dried and burnt in great heaps."

Accompanying the pain feeling—and even at times replacing it—there may be a stimulation of one of the special senses. In literary descriptions of painful experiences the language of some special sense is often used to describe the quality or intensity. Often it is in terms of color, and thus Homer refers to "black pains." In a minute analysis of this question Bleuler and Lehmann write: "Pains are never felt or recollected without their appropriate colors. They are colored variously, according to their intensity. Violent pains are accompanied by an idea of white; still more intense pains go from yellow to red and to dark brown; dull headaches give a tint which is almost black; darting pains, an idea of white dots; a pinch, a yellow tint, which is clearer the keener the pain is; indigestion, a more or less clear gray; colic a clear yellowish tint, which may pass over the red or brown." This phenomenon may of course be reversed, as in the old lady in Kipling's "They," whom certain colors "hurt."

In spite of differences in subjective description, there does exist an obvious variation in the pain reactions of individuals to what is, as near as possible, an identical stimulus. Common experience teaches, Critchley states, that the burly, lymphatic artisan feels pain less than the fragile artist or thinker. As Mrs. Browning put it, "the mark of rank in nature is capacity for pain." Precise data in the matter are scanty, however, although MacDonald some years ago made a careful psychometric study of pain sensitivity. His observations confirmed the general impressions by demonstrating a greater sensitiveness in the young than in the old, and in women than in men. Such generalizations are dangerous, however, and it remains problematic how, for example, men would stand the pangs of childbirth.

Indifference and insensitivity to pain is a matter of great interest. A marked degree of indifference has been associated by Lombroso with habitual criminals. Occasionally persons are seen who seem to possess such a high threshold for nociceptive stimuli that pain rarely, if ever, enters their experience. One of the best examples of unusual insensitivity was E. H. Gibson, known in American vaudeville as "the human pincushion."

At times pain contributes a pleasurable sensation. In such instances it is often closely bound up with religion and has been associated with a subtle process of refining or cleansing whereby the individual is exalted. Self infliction of pain may represent an effort to appease a sense of guilt or to atone for a misdeed. In

1. Waterston, David: Pain and the Mechanism of Its Production, Brit. M. J. 2:1087 (Dec. 15) 1934.
2. Critchley, Macdonald: Some Aspects of Pain, Brit. M. J. 2:891 (Nov. 17) 1934.

this connection the Biblical injunction is recalled: "If thy right hand offend thee, cut it off . . . and if thine eye offend thee, pluck it out." It is also possible that pain may be deliberately sought in order to relieve a more distressing discomfort or sensation. Here the action appears to be counterirritant, but the exact limits at which it becomes a sign of insanity are hard to define.

There are no words in English, Critchley says, to signify the state of mind that follows the cessation of a severe or protracted painful experience. The resulting emotional state of relief is perhaps attended by definite, even if transient, physical and psychologic gratification. Some psychologic concomitants of painful experience may linger after the pain has ceased. Thus, as Hugh Walpole wrote in his novel Hans Frost, "I am suffering tonight from toothache, and I have always noticed that a toothache is the most unintellectual pain in one's body, just as, in all probability, a stomachache is the most intellectual. Have you ever noticed, sir, how bright and clear one's brain becomes between the spasms of indigestion?" Many can, from their own experience, agree with one or both statements, but whether the clear headedness associated with some gastro-intestinal upsets is due to relief from pain or to starvation might well serve to inaugurate further investigation.

RECENT ADVANCES IN THE STUDY OF GANGRENE OF THE EXTREMITIES

Experimental and clinical research into the etiology of gangrene of the extremities occupies an increasingly important place in modern medicine. In this research the study of the larger vessels by morphologic methods has proved inadequate. Thus Herrman and Reid[1] have concluded that neither arteriographic examination nor morphologic studies of the large vessels can furnish a satisfactory explanation of the clinical manifestations. Rabinowitz[2] says: "While an outstanding lesion in thrombo-angiitis obliterans is a thrombotic closure of both large and small vessels, many clinical features of the disease cannot be attributed solely to this lesion." And now recent work by Popoff[3] throws new light on the limitation and inadequacy of morphologic research confined mainly to the state of the large vessels of the extremities.

In his studies on the digital vascular system, Popoff pays particular attention to the peripheral arteriovenous anastomosis in inflammation, arteriosclerotic gangrene, diabetic gangrene, obliterating thrombo-angiitis and supernumerary digits in man. These arteriovenous anastomoses were discovered by Sucquet in 1862 and again by Hoyer in 1887, and they are recognized now as a normal constituent of the peripheral vascular system. Popoff gives a detailed description of the anastomoses and discusses their function, which is controlled by local and general vasomotor mechanisms. According to his description, peripheral arteriovenous anastomoses or, as he calls them, the digital glomus or digital glomic system, serve two functions, one local and the other general. If the digits are exposed to cold it is through the agency of the glomic system that local temperature is maintained and even raised. This is accomplished by diverting blood from the capillaries and rushing it through anastomoses into collecting veins with a highly developed surface area. The glomic system also forms an important factor in the mechanism regulating the general temperature of the body. When fully opened it aids the dispersal of heat by allowing an enormous flow of blood to pass through the digits. The glomic system is not found in premature infants. To this Popoff attributes their poor control of the temperature of the body. No glomic system is found in cold blooded animals. In man, with the advance of age, the glomic system undergoes atrophy and in old age it may disappear completely. Comparative studies by Popoff on the glomic system in arteriosclerotic and diabetic gangrene indicate that in arteriosclerosis the destruction of the glomic system is due primarily to sclerosis of the afferent artery of the glomus, while in diabetes the arteriovenous anastomosis itself is involved first and this leads later to the destruction of the glomus. In both cases functional incapacitation of the glomic system is sufficient to cause the trophic changes in these diseases. Thus, according to this concept the neurovascular and trophic changes in the digits of arteriosclerotic patients and persons with diabetes may be due primarily to changes in the glomic system and not to inflammatory, degenerative or obstructive changes in the large arteries.

Popoff also offers a new concept of the etiology of obliterating thrombo-angiitis. In the cases of thrombo-angiitis that he studied he found in the digits abnormal arteriovenous communications or anastomoses that are different from the normal arteriovenous anastomoses just discussed. These abnormal anastomoses are found in the peripheral network of the digital vascular system. By diverting blood directly and continuously into the veins they diminish seriously the amount flowing from the capillary bed. As a result of this self-limited circulatory disturbance, the peripheral tissues of the digits suffer chronic and unrelievable anoxia with consequent development of the trophic changes and other manifestations characteristic of obliterating thrombo-angiitis. Both arteries and veins of the affected extremity undergo structural changes and, depending on the duration of the disease and the size of the abnormal arteriovenous anastomoses, the entire vas-

1. Herrman, L. G., and Reid, M. R.: The Conservative Treatment of the Arteriosclerotic Peripheral Vascular Diseases, Ann. Surg. **100**: 750 (Oct.) 1934.
2. Rabinowitz, H. M.: Newer Concepts on the Physiotherapy and Treatment of Thrombo-Angiitis Obliterans, Am. J. Surg. **21**: 260 (Aug.) 1933.
3. Popoff, N. W.: The Digital Vascular System with Reference to the State of the Glomus in Infection, Arteriosclerotic Gangrene, Diabetic Gangrene, Thrombo-Angiitis Obliterans and Supernumerary Digits in Man, Arch. Path. **18**: 295 (Sept.) 1934.

cular system of the body may show signs of involvement. This concept of the centripetal spread of obliterating thrombo-angiitis with the vascular anomaly as a causative agent is new and, if Popoff's results are corroborated, the nature of the disease will receive a new explanation.

THIRTIETH ANNIVERSARY OF THE COUNCIL ON PHARMACY AND CHEMISTRY

February 11, the Council on Pharmacy and Chemistry will complete its thirtieth year of service to the medical profession. For nearly a third of a century it has made contributions of inestimable value to rational therapeutics. Unique at its inception in 1905, it has no successful counterpart outside the United States. It has moreover served as a model for the Council on Physical Therapy and the Committee on Foods of the American Medical Association and for the Council on Dental Therapeutics of the American Dental Association.

Of the personnel of the Council, which serve entirely without remuneration, four members have been active ever since the meeting in Pittsburgh on Feb. 11, 1905, when the organization of this group was perfected. The secretary during the greater part of this period, W. A. Puckner, performed a notable service to medicine for twenty-seven years, until his death in 1932.

A comparison of the conditions prevailing in the marketing of drugs in this country before 1905 and those obtaining today indicates the debt that American medicine owes to the Council on Pharmacy and Chemistry. The rules governing the acceptance or rejection of remedies adopted in the beginning have gradually been amplified and clarified to meet new conditions. Thus the use of secret, ineffective and irrational preparations has decreased notably; advertising claims employed by manufacturers of pharmaceuticals for products accepted by the Council have attained standards of accuracy and truthfulness unequaled in any other field of marketing. THE JOURNAL and many other medical publications in this country, including the journals of all the state associations with the exception of Illinois, accept advertising for Council-accepted or official drugs only. But the Council's work would have come to naught had it not been for the militant aid of THE JOURNAL and the ever increasing support of the medical profession. True, many physicians still prescribe secret or semisecret or irrational preparations under the spell of persuasive, if unfounded, advertising claims made by certain manufacturers. But these clinicians are decreasing in number; more and more does the practitioner meet the claims of the detail man for a new pharmaceutical with the question "Is it accepted by the Council?"

Among the important contributions of the Council have been the evaluation of new drugs on the basis of available evidence, the publication of reports giving the results of this evaluation, the standardization with the assistance of the A. M. A. Chemical Laboratory of products that show promise of therapeutic usefulness, and the publication of special articles in review of subjects of current interest to the medical profession. A notable example of the latter is the series on Glandular Physiology and Therapy, which begins in the present issue of THE JOURNAL. In addition the Council issues several books: New and Nonofficial Remedies (revised yearly), Useful Drugs, the Epitome of the U. S. Pharmacopeia and National Formulary, and (in cooperation with the Council on Medical Education and Hospitals) Hospital Practice for Interns. It is impossible to present adequately, in so brief a compass, all the valuable services of the Council, which have made themselves felt wherever medicine is practiced throughout the civilized world. It continues its important tasks, ever increasing in number and volume, unselfishly and with intelligence and foresight. It merits unfailing support by the medical profession.

Current Comment

ASBESTOSIS

The nature of the effects of silica dust expressed in the term "silicosis," with the resultant extraordinary predisposition to pulmonary tuberculosis, is well known. Some of the more cogent etiologic, metabolic and legal aspects of this condition have been discussed in these columns.[1] These important developments in the study of lung diseases due to the inhalation of dust have now been extended in this country [2] to the pneumonoconiosis caused by asbestos dust and termed "asbestosis." This preliminary study of the asbestos industry presents data obtained from an examination of dust conditions in five asbestos fabricating plants along the Atlantic seaboard. The investigation included physical examinations of asbestos workers, together with x-ray films, and a consideration of the dust exhaust systems designed to eliminate asbestos dust. It appears evident that prolonged exposure to this dust causes a pulmonary fibrosis demonstrable on x-ray films. This condition appears to be of a type different from silicosis and somewhat milder. Furthermore, a predisposition to tuberculosis due to asbestos dust was not indicated in this study. There were, however, cases of definite cardiac enlargement frequently associated with the asbestosis. The authors propose valuable recommendations, which include a thorough physical examination of prospective employees and suggestions for the control of dust hazards in the industry. Equally important is the proposal that the manufacturers sponsor studies of known cases of asbestosis as well as investigations on effects of the condition on the heart and the circulation. A more detailed report of the asbestos industry in the United States will undoubtedly provide further

1. Absorption and Excretion of Silica, editorial, J. A. M. A. **102**: 1303 (April 21) 1934; Protection Against Dusts, ibid. **103**: 1543 (Nov. 17) 1934.

2. Lanza, A. J.; McConnell, W. J., and Fehnel, J. W.: Pub. Health Rep. **50**: 1 (Jan. 4) 1935.

illuminating information on the nature of the occupational hazard encountered in this industry and the measures that should be taken to prevent or control this condition.

Medical Economics

WORKMEN'S COMPENSATION IN NEW YORK AND PENNSYLVANIA

Reports of committees on workmen's compensation in the states of New York and Pennsylvania respectively have recently been published.[1] These reports give an opportunity for judgment on a little more than twenty years' experience with workmen's compensation legislation in two large industrial states. The New York committee was composed entirely of physicians. The Pennsylvania committee contained two physicians out of seven members but also had an advisory committee of nine, seven of whom were physicians.

It is significant that in both cases the least satisfactory features of the operation of the law were in the provisions for medical care. It is fair to draw the conclusion from these reports that this weakness is largely due to the fact that there was little or no consultation with the medical profession at the time the laws were enacted. It is also worthy of note that among the more important recommendations of both committees is a wider participation of the medical profession in the administration of the provisions for medical care.

The New York committee subdivided the abuses in the operation of the law into "those over which the medical profession had at present no control and those directly attributable to the medical profession." Those which are beyond the control of the medical profession are listed as:

1. The hiring of cheap and incompetent medical service by employers and insurance carriers.
2. Reduced charges by hospitals in order to obtain cases.
3. "Lifting."
4. Errors in causal relationship, where carriers have frequently attempted to prove wrongly that patients were malingering or where awards had been made by lay referees for conditions which had no relationship to the antecedent injury or occupation, or where a lay referee attempted to evaluate opposing medical testimony of experts employed by the interested parties.
5. Postponement of compensation awards.
6. Other legal injustices, most of which were also due to the control of the physician and medical records by an employer or an insurance carrier.

Another set of abuses were ascribed to the medical profession. These are listed as:

1. Inefficient medical treatment due to a failure to refer cases to a specialist when such treatment was needed.
2. Overtreatment and overcharging.
3. Prolonged period of compensation due to the fact that physicians "have occasionally conspired with injured workmen to obtain compensation for him for a longer period than his injury warranted."
4. Prolonged physical therapy.
5. Inadequate medical testimony.
6. Medical advertising and racketeering in order to secure cases.

The committee submits a series of recommendations to remove these abuses. The first is a "limited free choice of physician by the employee." It is also recommended that opportunity be given for transfer of cases when this is found desirable and that the county medical society "function as the fact finding agency on professional conduct and professional competence."

Furthermore, it is recommended in the New York report that medical fees should be standardized by the medical society and arrangements made for the arbitration of disputed bills for medical service; medical practice by insurance carriers should be eliminated and there should be greater supervision of self insurers. The lay referees who are to determine disability should have the right to avail themselves of expert medical opinion, and for this purpose a medical advisory and appeal board should be set up.

The Pennsylvania report is based on a very extensive study in which as many as 125 workers, paid through the C W A, investigated more than 7,000 workmen's compensation cases. There is a close resemblance between the medical recommendations of the committees in these two states. The Pennsylvania committee, however, urges that the present inadequate provisions for medical care of the Pennsylvania law be extended. It also urges at least a limited free choice of physician, wider opportunities for consultation and provision for impartial medical opinion.

This report contains an extensive and valuable graphic presentation of the features of the Pennsylvania compensation law in comparison with the laws of other states. There is considerable criticism of the self-insurance provisions of the law, although it is recognized that much of this criticism applies to only a minority of the self insurers.

Of the 7,000 cases studied, about "70 per cent of the persons interviewed expressed belief that they had received fair treatment. The others complained of delay, unfairness, and the necessity of litigation." They also complained of inadequate medical treatment and it was shown that more than two thirds were treated over a period of two months or longer, and one fourth required medical treatment for four months or longer, although the law provides treatment for only thirty days.

It would seem to be a fair summary of the two reports to state that, in the opinion of these committees, absence of medical advice in the formation of the law and dominance of lay interests, often seeking financial advantage, had defeated many of the purposes of the law, especially in regard to medical service. There is unanimous agreement that improvement in the medical service and in the other features of compensation which depend on that service must be based on a much wider participation of the medical profession and medical societies.

1. Report of Governors Committee on Workmen's Compensation, Pennsylvania Labor and Industry 21:4 (Nov.) 1934. Report of Committee on Workmen's Compensation appointed by Governor Herbert H. Lehman of New York.

Association News

SPECIAL SESSION OF HOUSE OF DELEGATES AT CHICAGO, FEBRUARY 15

Reduced Railroad Rates for Return Tickets

Special rates have been granted by various passenger associations for the benefit of the members of the Annual Congress on Medical Education, Hospitals and Licensure and the Special Session of the House of Delegates in Chicago.

To have the benefit of a return rate of one-third fare, it will be necessary for each member to secure a Certificate from the railroad ticket agent when he purchases his ticket to Chicago. When the Certificate has been certified to and validated at the Palmer House in Chicago, it will entitle its holder to purchase a return ticket to his home, over the same route traveled to Chicago, at one-third fare.

MEDICAL BROADCASTS

Columbia Broadcasting System

The American Medical Association broadcasts on a western network of the Columbia Broadcasting System each Thursday afternoon on the Educational Forum from 4:30 to 4:45, central standard time. The next three broadcasts will be delivered by Dr. W. W. Bauer. The titles are as follows:

February 14. Heart Valves.
February 21. Heart Muscles.
February 28. Protecting the Heart.

National Broadcasting Company

The American Medical Association broadcasts under the title "Your Health" on a Blue network of the National Broadcasting Company each Tuesday afternoon from 4 to 4:15, central standard time. The next three broadcasts will be as follows:

February 12. What the Public is Thinking About Health, W. W. Bauer, M.D.
February 19. Rheumatism and Gout, Morris Fishbein, M.D.
February 26. Health and Education, Morris Fishbein, M.D.

Special Coast to Coast Broadcast

The American Medical Association will broadcast on a special program arranged through the courtesy of the National Broadcasting Company over a network of stations, beginning at 6 p. m., eastern standard time, Monday, February 18. The program will include music and three speakers from among physicians in attendance at the Annual Congress on Medical Education and Medical Licensure, meeting in Chicago on that day. The speakers will be introduced by Dr. Morris Fishbein. The speakers and their topics are as follows:

Advancement of Medical Education, Walter L. Bierring, M.D.
The Prolongation of Life, Ray Lyman Wilbur, M.D.
The Battle Against Tuberculosis, Kendall Emerson, M.D.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION, PUBLIC HEALTH, ETC.)

ALABAMA

Bills Introduced.—H. 30 proposes to prohibit cities and towns of from 15,000 to 20,000 population from collecting occupational taxes on physicians practicing within their jurisdictions. S. 26 proposes to authorize the sexual sterilization of certain socially inadequate inmates of state institutions.

ARIZONA

Bill Introduced.—S. 15 proposes to repeal the laws regulating the distribution and possession of narcotic drugs and to enact what apparently is the uniform narcotic drug act.

ARKANSAS

Bill Passed.—S. 126, to supplement the medical practice act, has passed the senate, proposing that licentiates of the eclectic medical examining board shall register annually with that board and pay at that time a registration fee of $2. Failure of an eclectic licentiate to register within the time stated is to suspend automatically his right to practice, and a failure to register for three consecutive years shall automatically cancel his license to practice.

Bills Introduced.—H. 15 proposes to require any physician treating a person suffering from a gunshot, pistol or bullet wound to report that fact immediately to the appropriate police authorities. H. 105, apparently to supplement the pharmacy practice act, proposes (1) to define drugs as "any drug or compound listed in the United States Pharmacopeia or National Formulary, or both, which are [sic] used for the prevention, mitigation, or cure of disease"; (2) to prohibit the distribution of drugs, as defined, except by registered pharmacies; (3) to permit the board of pharmacy to enjoin the operation of any store not complying with the pharmacy laws. H. 110 and S. 67 propose to repeal the laws regulating the possession and distribution of narcotic drugs and to enact what the draftsmen of these bills cite as the "uniform narcotic drug act." The bills, however, differ from the model uniform narcotic drug act in some important particulars and contain obvious errors in phraseology. They omit the provisions in the model bill intended to limit the gross quantity of a habit-forming drug a person can buy in exempt preparations within a period of forty-eight hours. S. 142 proposes that all persons who have engaged in the practice of medicine for twenty years continuously prior to Jan. 1, 1935, shall, on presentation of such proof, be entitled to registration by the eclectic medical examining board. H. 82 proposes to provide compensation to workmen for injuries and occupational diseases or infections arising out of or in the course of their employment. The employer is to be required to furnish such medical, surgical and other attendance or treatment, nursing and hospital services, and medicines, crutches and apparatus, for such period as the nature of the injury or the process of recovery may require. Apparently the employer is to have the right to designate the physician and the hospital that are to treat or care for the injured employee. If the employer does not provide the services referred to after request by the employee, the employee may obtain them himself at the employer's expense. H. 172 proposes to make it unlawful for a corporation to keep for its own benefit any unused portion of sums collected from its employees to provide them with medical services. It is to be the duty of such a corporation to refund quarterly to its employees any accumulation of such funds not necessary to keep the medical service plan in operation. H. 189 prohibits the sale of barbituric acid derivatives and/or compounds thereof except on the prescription of a licensed physician. S. 107 proposes that all persons who have been engaged in the practice of medicine twenty years continuously prior to Jan. 1, 1935, on presentation of such proof be licensed by the homeopathic board, by the eclectic board or by the nonsectarian board of medical examiners, according to the applicant's school of practice.

CALIFORNIA

Special Meeting Called for House of Delegates.—To formulate principles and policies on pending and proposed federal and state legislation related to medical care and medical services, a special meeting of the house of delegates of the California Medical Association has been called for March 2 in Los Angeles.

Bills Introduced.—A. 246 proposes to authorize the organization of corporations to provide on a nonprofit basis hospital care for their members and to exempt such corporations from the requirements of the state insurance law. The funds of a corporation organized under the provisions of this bill are to be exempt from all forms of state, county, municipal and school taxes. Such a corporation is specifically prohibited from in any manner providing medical service "in connection with the diagnosis or treatment of disease as controlled or prescribed by the medical practice act of the state of California or in any manner whatsoever engaging in the corporate practice of medicine and/or dentistry." A. 255 proposes that the expert medical witnesses and the medical examiners whom the law permits a court to appoint to testify in a pending case shall be selected from a list of qualified physicians, prepared by the civil service commission after consultation with the state board of medical examiners, the medical director of the industrial accident commission, the deans of the medical schools of the University of California and of Stanford University, and the judicial council. A. 429 proposes that every public and private school be so equipped as to render first medical aid to injured students. S. 154, to amend the medical practice act, proposes (1) that a licentiate appealing from a judgment of the board of medical examiners revoking or suspending his license or placing him on probation must file with the clerk of the court a surety bond for $250 to secure payment of the costs of appeal; and (2) to make the following acts additional causes for the revocation or suspension of licenses: (*a*) fraudulent representation that a manifestly incurable condition can be cured, (*b*) advertising that the licentiate will treat syphilis or prostate conditions or prostatic ailments, (*c*) the execution by a licentiate in his professional capacity of any false certificate, and (*d*) acceptance by a licentiate of employment from persons who directly or indirectly solicit patients. S. 155, to amend the medical practice act, proposes to permit the issuance of a physician's and surgeon's certificate to an applicant who has completed three years' study in a medical school and has served at least one year's internship. S. 311, to amend the laws regulating the sale, possession, distribution and use of narcotic drugs, proposes that, in addition to any other penalty, any person convicted of unlawfully distributing narcotic drugs, who is not himself a drug addict, may be subject to from one to twenty lashes at a whipping post.

COLORADO

Annual Registration Due Before March 1.—Every person licensed to practice any form of the healing art in Colorado is required by law to register annually before March 1, with the secretary-treasurer of the board of medical examiners, and to pay a fee of $2 if a resident of Colorado, or $10 if a nonresident. Failure to pay this fee within the time stated automatically suspends the right of a licentiate to practice while delinquent. If he nevertheless continues to practice he is subject to the penalties provided by law for practicing medicine without a license. Failure to pay this fee for three consecutive years results in the automatic cancellation of a delinquent practitioner's license to practice.

Bills Introduced.—S. 699, to amend the workmen's compensation act, proposes that if an employee or his representative is awarded compensation under the act no action may thereafter be brought against the physician who treated the industrial injury which was the basis of the award. S. 700 proposes that every contract by which a hospital or a licensed practitioner of the healing art warrants or guarantees the specific result of treatment or care to be given any patient shall be void unless such contract or some note or memorandum thereof be in writ-

ing and be signed by the party sought to be charged therewith. S. 701 proposes that all actions for malpractice against a hospital must be instituted within two years after the accrual of the cause of action.

CONNECTICUT

Bill Introduced.—H. 28, to amend the chiropody practice act, proposes to define chiropody, or podiatry, as "the diagnosis of foot ailments and the practice of minor surgery upon the feet, limited to those structures of the foot superficial to the inner layer of the fascia of the foot; the dressing, padding and strapping of the feet; the making of plaster models of the feet and the palliative and mechanical treatment of functional disturbances of the feet as taught and practiced in the schools of chiropody recognized by the examining board."

Lectures on Social Aspects of Medicine.—The department of public health of Yale University School of Medicine is sponsoring a series of lectures in New Haven dealing with the backgrounds of medical practice. Dr. Henry E. Sigerist, director of the Institute of the History of Medicine, Johns Hopkins University, Baltimore, opened the series with three lectures on the development of medicine in relation to changing social conditions, January 14, 15 and 17. These lectures on the social aspects of medicine are designed especially for students of medicine but will also be open to the public. The department of public health has for some time been interested in furthering the investigation of the social backgrounds of disease in individual patients. According to an announcement, the work has been developed under the direction of Ira V. Hiscock, C.P.H., professor of public health, to the point at which a more comprehensive survey of the many aspects of American life, as they pertain to health problems, is now thought desirable. The work on social backgrounds has been conducted with the cooperation of various agencies, including the social agencies of New Haven, the city department of health, the social service department of the medical school, and more recently the social science division of the Institute of Human Relations at Yale.

DELAWARE

Bill Introduced.—H. 38, to amend the workmen's compensation act, proposes to make compensable "any injury or disease arising out of and in the course of the employment as well as such disease or infection as naturally results directly therefrom when reasonably treated."

Society News.—Dr. Abraham Cantarow, Philadelphia, addressed the New Castle County Medical Society in Wilmington, January 10, on "Practical Aspects of Specific and Nonspecific Calcium Therapy." Dr. William H. Speer, Wilmington, addressed the society, Dec. 18, 1934, on "The Injection Treatment of Varicose Veins."

ILLINOIS

Bills Introduced.—H. 96 proposes to impose a tax of 10 per cent of the gross cash receipts from sales in Illinois on persons manufacturing patent and proprietary medicines in the state. H. 97 proposes to authorize the sexual sterilization of insane, feebleminded, mentally defective, idiot, imbecile or epileptic inmates of state institutions. H. 44 proposes to repeal the laws regulating the distribution and possession of narcotic drugs and to enact what apparently is the uniform narcotic drug act. H. 109 proposes to accord liens to physicians and hospitals treating persons injured through the negligence of others, on all rights of actions, suits, claims or demands accruing to the injured persons because of their injuries.

District Meeting.—The Iowa and Illinois Central District Medical Association held its quarterly meeting at the Blackhawk Hotel in Davenport, Iowa, January 11. The president, Dr. John C. Souders, Rock Island, gave a tribute to Dr. George L. Eyster, who practiced medicine in the community for fifty-five years and who now lives in Coral Gables, Fla. Other speakers were Drs. Merrill M. Benfer, Davenport, on "Consideration in the Treatment of Hypertrophied Prostate"; William H. Olmstead, St. Louis, "Vascular Diseases of the Extremities," and Louis G. Herrmann, Cincinnati, "Recent Advances in the Treatment of Obliterative Arterial Diseases of the Extremities." Several patients with arterial disease of the extremities were presented at this meeting.

Chicago

Malaria Among Narcotic Addicts.—The use of the same syringe by several narcotic addicts was said to be the cause of an outbreak of malaria recently. Five deaths from the disease in the county hospital prompted a raid on the hotel where two of the victims lived. Two of the men arrested were found to be potential malaria carriers, having had the disease several years ago. They confessed to being part of a group of addicts that usually met together and used the same syringe.

Society News.—A symposium on transurethral resection constituted the program of the Chicago Urological Society, January 24; speakers were Drs. Edward W. White, Harry Culver, Herman L. Kretschmer and Irvin S. Koll.——Dr. Royd R. Sayers of the U. S. Public Health Service, Washington, D. C., discussed "Silicosis as a Factor in Compensation and Personal Injury Cases" at a meeting, January 26, sponsored by the hospitality committee of the Chicago Bar Association. Members of the Chicago Medical Society and the Chicago Society of Industrial Medicine and Surgery were invited.—— The Chicago Medical Society held a memorial meeting, January 27, in honor of its members who have died in the past year. In addition to a musical program, Dr. William Allen Pusey discussed "Medicine the Last Fifty Years and the Next Fifty," and Frederick F. Shannon, pastor of the Central Church, "Some Doctors I Have Known."—— Dr. George W. Crile, Cleveland, addressed the Public Affairs Round Table of the Union League Club of Chicago, January 25, on "Medical Research, Health and Longevity." This lecture accompanied the first showing of the sound motion picture "That Man May Live," prepared by the American College of Surgeons.

INDIANA

Bills Introduced.—H. 113 proposes to authorize the state board of pharmacy to appoint a narcotic inspector to enforce, and to collect information necessary to enforce, the state and federal laws relating to narcotic drugs. S. 83 proposes to repeal the laws regulating the distribution and possession of narcotic drugs and to enact what apparently is the uniform narcotic drug act. S. 118, to amend the workmen's compensation act, proposes (1) to make occupational diseases compensable, and (2) that no physician be permitted to testify at any hearing provided for in the act or in any action at law brought against an employer who is subject to the act, unless, at the time of making his report to the party employing him, he shall also furnish the opposite party with a copy of the report, setting out in detail the history, complaints and findings. H. 211 proposes to authorize counties, cities and towns to supply insulin free of charge to citizens who are in need of insulin treatment for diabetes and who are financially unable to purchase the drug.

IOWA

Bill Introduced.—S. 20 proposes that before any applicant for a license to practice medicine, osteopathy, osteopathy and surgery or chiropractic may be examined by his professional board he must first pass an examination before an impartial basic science board in anatomy, physiology, chemistry, pathology, bacteriology and hygiene. The basic science examining board is to consist of five members of the faculties of the State University, the State College of Agriculture and Mechanic Arts, the Iowa State Teachers College and any other university or college accredited by the Iowa state board of educational examiners. All members of the board must be learned in the basic sciences and no member may be licensed to practice any of the healing arts.

LOUISIANA

Centennial Celebration at Tulane.—The one hundredth anniversary of the establishment of Tulane University of Louisiana School of Medicine, New Orleans, was commemorated in a program sponsored by the Orleans Parish Medical Society, January 7. This observance is a forerunner of the celebration planned by the university in June for three or four days, culminating on commencement day, June 12. The recent program marked the actual day of its founding, the first Monday in January 1835. The history of the institution was reviewed by Mayor T. Semmes Walmsley, and Drs. Charles C. Bass, dean, Waldemar R. Metz, Albert E. Fossier and Rudolph Matas.

MARYLAND

Bills Introduced.—H. 36, to amend the workmen's compensation act, proposes to eliminate those provisions in the present law which define the evidence that must be submitted in order to permit recovery of compensation for hernia. H. 53 proposes to require both parties to prospective marriages, as a condition precedent to obtaining licenses to wed, to present certificates from licensed physicians that both parties are free from contagious disease.

MASSACHUSETTS

Personal.—Dr. Edward B. Lane, Boston, has resigned as medical superintendent of an institution for mild nervous disorders, after twenty-five years' service. He has been succeeded by Dr. James Martin Woodall.——Dr. James B. Atwater, Westfield, resigned as chief of staff of the Noble Hospital, Nov. 24, 1934, after twenty-seven years' service; he was made chief emeritus and Dr. Edward S. Smith was appointed to succeed him.

Bills Introduced.—H. 358 proposes to authorize the department of mental diseases to construct a hospital for drug addicts on Rainsford Island, in the city of Boston. H. 1736 proposes to prohibit the distribution of any article intended as a sex inciting device or contrivance and to prohibit the distribution, except by physicians or pharmacists, of any article intended to be used for the prevention of venereal disease. H. 1400 proposes a system of compulsory and voluntary sickness insurance. The benefits proposed consist of cash and all forms of medical and dental service. Persons employed at "other than manual labor" and receiving wages in excess of $60 a week, farm laborers, and persons employed by an employer having less than three employees in personal or domestic services, are excluded from the compulsory insurance of the bill but are entitled to participate in the voluntary insurance.

MICHIGAN

Bill Introduced.—H. 92, to amend the workmen's compensation act, proposes to make compensable "all disabilities or death suffered by an employee as a result of occupational injury or disease."

Detroit Health Council.—The creation of a Metropolitan-Detroit Health Council to secure good health service for all the people at a minimum of expense was unanimously endorsed at a meeting of the Wayne County Medical Society, Dec. 17, 1934. It was recommended that the officers of the society be empowered to effect this organization in cooperation with community agencies dealing with medical service and health protection. About 400 members of the society attended the meeting. Following a discussion of medical economics, William J. Burns, executive secretary of the society, outlined the plans for the organization of the health council, and Dr. Charles Godwin Jennings introduced the resolution that recommended its creation.

MINNESOTA

Lectures for Teachers' Colleges.—The Minnesota State Medical Association, cooperating with the Minnesota Public Health Association, is providing a health lecture course for the teachers' colleges of the state. The course consists of a series of five lectures, one each month, by prominent physicians of the state. The titles of the lectures are Milestones of Medicine, Youth's Greatest Enemy, That Heart of Yours, Heritage of Health, and Your Senses and You.

Bills Introduced.—H. 86 proposes to authorize the sexual sterilization of inmates of state institutions who are afflicted with mental deficiency, perversion, marked departures from normal mentality or from disease of a syphilitic nature, likely to be transmitted to descendants. S. 145 proposes to amend the law prohibiting the procuring of an abortion or miscarriage. The present law permits the use of any means to procure a miscarriage if "the same is necessary to preserve" the life of the woman. This bill proposes to permit also the procuring of a miscarriage if it is necessary to preserve the life of the fetus. S. 177 proposes to provide for the licensing of dental hygienists by the board of dental examiners. A dental hygienist is to be authorized to remove lime deposits, accretions and stains from the exposed surfaces of the teeth, administer gas, ether and general anesthesia, and to make instrumental examination of the teeth or cavities. A dental hygienist, however, must operate (1) in the office of a licensed dentist and at all times under his direct supervision or (2) in a public institution or school if at all times under the general supervision of a licensed dentist. H. 212 proposes to require every physician or the governing authorities of every hospital, on treating persons suffering from gunshot or knife wounds, to report the facts immediately to the proper police officials.

MISSOURI

Physical Therapy Committee Appointed.—At the annual meeting of the council of the Missouri Medical Association in Columbia, Nov. 19, 1934, the organization of a committee on physical therapy was approved. Drs. Alexander J. Kotkis and Frank H. Ewerhardt, St. Louis, were named members of the committee, with three other members to be appointed later.

Bills Introduced.—S. 28 proposes to make it unlawful for any person to cultivate, cure, prepare, distribute in any manner or possess marijuana. Physicians, dentists and osteopaths, however, are to be permitted to prescribe marijuana. H. 174, to amend the workmen's compensation act, proposes, in effect, to permit chiropractors and osteopaths to render the medical and surgical treatment called for in that act.

MONTANA

Bill Passed.—S. 35, to supplement the pharmacy practice act, has passed the house, proposing to authorize the state board of pharmacy to adopt rules requiring registered pharmacists to keep a record of all poisons sold or disposed of, containing the signatures of the purchasers and such other information as may be required by the board.

Bill Introduced.—H. 86, to amend the chiropractic practice act, proposes (1) to define chiropractic as "the science that teaches that disease results from anatomic disrelation and teaches the art of restoring anatomic relation by adjustment by hand and the use of such other physical, thermal and electrical methods and modalities as are necessary to the restoration of proper anatomic relation," and (2) to require a chiropractic licentiate to show as a condition precedent to his right to annual reregistration that during the past year he has attended a postgraduate course in a recognized chiropractic college or has attended at least one of the "educational" programs as conducted by the Montana chiropractic association.

NEBRASKA

Bills Introduced.—H. 143 proposes to make it the duty of every physician, hospital or pharmacy treating any person suffering from any injury inflicted by a knife, gun, pistol or other deadly weapon, or by other means of violence, to report immediately to the appropriate police officials the name and address of the patient and the nature and extent of the injuries. S. 50, to amend the optometry practice act, proposes, among other things, to define optometry as "the science of diagnosing disturbances of the visual apparatus and functions." H. 137 and H. 147 propose to repeal the laws regulating the distribution and possession of narcotic drugs and to enact what apparently is the uniform narcotic drug act. H. 230 proposes a system of compulsory and voluntary sickness insurance. The benefits proposed consist of cash and of all forms of medical and dental services. Persons employed at "other than manual labor receiving wages in excess of $250 monthly," farm laborers, and persons employed by an employer having less than three employees in personal or domestic services, are excluded from the compulsory insurance of the bill but are entitled to participate in its voluntary insurance.

NEW HAMPSHIRE

Bills Introduced.—H. 143 proposes to make it the duty of pensation act, among other things proposes to require the employer to furnish to an injured employee, without limit as to time or amount, reasonable medical and hospital services and other remedial care. H. 196 proposes to limit the administration of anesthetics to licensed physicians and dentists. It proposes also to prohibit the administering of an anesthetic unless a responsible adult third person is present at the administration and during the period the patient is under the anesthetic. H. 270, to amend the chiropody practice act, proposes to define a chiropodist as "one who examines, diagnoses, or treats medically, mechanically, surgically, or by electrical and manipulative means, or by bandaging and strapping, the ailments of the human foot, not requiring the use of anesthetics other than local." H. 153 proposes to accord to hospitals, caring for persons injured through the fault of others, liens on all rights of action, claims, judgments, settlements or compromises accruing to the injured persons by reason of their injuries.

NEW JERSEY

Bill Introduced.—S. 50 proposes to authorize the sexual sterilization of idiot, epileptic, imbecile and feebleminded inmates of state institutions.

Surgeons' Annual Meeting.—Dr. Briscoe B. Ranson Jr., Maplewood, was elected president of the Society of Surgeons of New Jersey at Newark, January 9. Speakers included:

Dr. George W. Crile, Cleveland, The Adrenal Sympathetic System and Its Diseases.
Dr. Arthur H. Curtis, Chicago, Obstructive Lesions of the Uterus and Their Complications.
Dr. Walter E. Dandy, Baltimore, Diagnosis and Treatment of Disturbances of the Cranial Nerves.
Dr. Philip D. Wilson, New York, Injuries in the Region of the Elbow.
Dr. Henry Bugbee, New York, Present Status of the Prostatic Problem.
Dr. William Wayne Babcock, Philadelphia, Management of Carcinoma of the Large Bowel.

NEW MEXICO

Bill Passed.—H. 57 has passed the house, proposing to require the board of pharmacy to license, without examination, any licensed physician who owns or operates a drug store or any other business requiring the services of a registered pharmacist.

NEW YORK

Bills Introduced.—S. 401 proposes to prohibit the advertisement, display, sale or other disposal of appliances, drugs or medicinal preparations intended or having special utility for the prevention of venereal disease and/or used in gynecologic hygiene or treatments, except in places duly registered by the state board of pharmacy. S. 357 and H. 445 propose to safeguard the distribution of "dangerous caustic or corrosive substances," as defined in the Federal Caustic Poison Act, by requiring their labeling as poison. S. 344 proposes to amend that provision in the vital statistics law which requires that the personal particulars called for in a certificate of birth shall be authenticated by the signature of an informant, who may be any competent person acquainted with the facts, by providing that such personal particulars shall be obtained from such a person. A. 461, to amend the medical practice act, proposes to make it unlawful for any one other than a licensed physician to conduct, direct, supervise or control the work or reports of a clinical laboratory, which is defined as "a laboratory in which tests are made on individual persons, their secretions, excretions, blood and tissues, to aid in the diagnosis, prognosis, or treatment of the individual's physical or mental state or states." The provisions of this bill, however, are not to apply to qualitative or quantitative analysis of urine by a licensed pharmacist; or to a clinical laboratory director duly licensed to conduct, direct or supervise a clinical laboratory within the city of New York; or to any person who has conducted, directed or supervised a clinical laboratory in the state for a period of at least six months prior to the date this bill may become enacted. S. 409 and A. 551 propose that that portion of a street in front of a physician's residence, if properly marked, shall at all times be reserved as a parking space for the physician's personal use and for the use of persons visiting him professionally. A. 558 proposes to prohibit the employment of nurses by state, county or city hospitals or in hospitals supported in whole or in part by public funds, for more than eight hours in any one day.

New York City

Laboratory Service on Pneumonia.—The bureau of laboratories of the department of health has recently extended its diagnostic service for the typing of pneumococci by opening a branch laboratory for that purpose at Bellevue Hospital.

Study of Amebic Dysentery.—The U. S. Public Health Service reports a study of the occurrence of amebic dysentery in New York between Nov. 1, 1933, and Sept. 30, 1934. Before October 1933 dysentery was rarely reported in the city, only nineteen, twenty and twenty cases having been listed in 1930, 1931 and 1932. When a warning was received from the Chicago health department that an outbreak had occurred in that city, intensive studies were begun of all cases reported to the New York health department. Of 121 cases that occurred between Nov. 1, 1933, and Sept. 30, 1934, seventy-three, or 60.3 per cent, originated in Chicago. Of the remaining cases, thirteen apparently originated in New York, fifteen in places in the United States outside of Chicago and New York, and twelve in foreign countries. In eight instances the source of infection could not be traced. At the end of the period studied seventeen deaths had occurred, forty-one patients were said to have recovered and sixty-three were still undergoing treatment. The largest number of cases, twenty-seven, was reported in December 1933. The number of cases reported from January to September 1934, thirty-two, attributed to sources other than Chicago, affords a better indication of the normal incidence of dysentery in the city, the report concludes. Of the usual number a fairly constant percentage comes from foreign sources. The apparent increase over earlier years may be ascribed to greater interest or increased diagnostic skill on the part of physicians or to better reporting, it is noted.

NORTH DAKOTA

Bill Introduced.—H. 73 proposes to create a board of naturopathic examiners and to regulate the practice of naturopathy. According to the bill, "naturopathy, which includes physiotherapy, is defined to be: The treating of the human body for hygienic [sic] or remedial purposes by means of massage, baths, heat, light vibration, manipulation, nontoxic herbs and diet, as taught by Naturopathic Schools and Colleges."

OHIO

Columbus Credit Bureau.—The Columbus Academy of Medicine has authorized the establishment of a credit bureau to be known as the Columbus Bureau of Medical Economics, through which patients' credit ratings will be recorded and exchanged, and delinquent accounts will be handled. Dr. Eugene F. McCampbell has been named president and Dr. Russel G. Means, secretary.

Personal.—Dr. Gustav Eckstein Jr., Cincinnati, author of several novels and of "Noguchi," received the Sachs Prize of $500, given annually to a Cincinnatian who has made a notable contribution to art, literature, science or education.——Dr. and Mrs. Florus Fremont Lawrence, Columbus, celebrated their golden wedding anniversary, January 1. Dr. Lawrence was professor of surgery, anatomy and clinical surgery at the old Ohio Medical University; clinical lecturer in abdominal pelvic surgery at Starling Medical College, and in later years, 1906-1916, clinical lecturer on surgery at Ohio State University College of Medicine. In recent years he has been on the staffs of McKinley and White Cross hospitals. He is a former president of the Columbus Academy of Medicine.

OKLAHOMA

Bills Introduced.—H. 126 proposes to create a board of chiropody examiners and to regulate the practice of chiropody, which the bill defines as the examination, diagnosis or treatment manually, mechanically, medically or surgically of the ailments of the human foot, except the amputation of a toe or foot, and the use of anesthetics other than local. H. 101 proposes to amend the laws relating to divorce by permitting a divorce when either spouse has been adjudicated insane and has been confined in an institution for treatment for three years or more.

OREGON

Bills Introduced.—H. 57, to amend the laws relating to taxation, proposes to deny exemption from taxation to any incorporated hospital which makes a charge for its services, on the ground that such a hospital is a noncharitable institution. H. 85 proposes to repeal the law requiring applicants for marriage licenses to present medical certificates showing their freedom from venereal and certain other communicable diseases and certain inheritable diseases and conditions.

Bill Passed.—H. 112, to amend the medical practice act, has passed the house. It proposes (1) to permit the medical examining board to hold meetings for examinations whenever it deems them advisable, provided such meetings are held at least twice each year, the present law requiring that meetings for examination be held on the first Tuesdays of January and July, (2) to permit the board to suspend licenses as well as to refuse to issue or to revoke them for the causes now stated in the law, and (3) to add to the conduct which shall be deemed to be "unprofessional or dishonorable conduct" "the obtaining of any fee through fraud or misrepresentation."

PENNSYLVANIA

Survey of Maternal Health.—The Medical Society of the State of Pennsylvania through its commission on maternal welfare is undertaking a complete survey of the problem in the state. Dr. James S. Taylor, Altoona, chairman of the commission, has asked each county society to appoint a local committee, whose chairman will become a member of the councilor district committee, and the chairman of the district will in turn be a member of the commission.

Bills Introduced.—H. 187 proposes an amendment to the constitution to permit the general assembly to establish a system of compulsory health insurance. H. 188 proposes to establish a system of compulsory health insurance in favor of all persons engaged in manual labor and all other employed persons earning $50 a month or less. The proposed benefits, in case of illness or accident, consist of necessary medical, surgical, dental, nursing and hospital attendance and treatment, available alike to the employed person and to the dependent members of his family. H. 271 proposes to authorize the establishment of a state tuberculosis sanatorium in one of the state forest reservations.

Philadelphia

Neurologic Society Fifty Years Old.—The Philadelphia Neurological Society celebrated its fiftieth anniversary, January 22, with a meeting at the headquarters of the College of Physicians of Philadelphia. Dr. William G. Spiller read a paper on "Fifty Years of Psychiatry," and Dr. Charles H. Frazier one on "Neurosurgical Activities of Members of the Philadelphia Neurological Society."

Bequest to Pennsylvania Hospital.—Mrs. Henrietta Dallas Pepper, a great-great-granddaughter of Benjamin Franklin, left the greater part of her $200,000 estate to the Pennsylvania Hospital to establish a ward "for persons of gentle birth but unable to pay," according to newspaper reports. The ward is to be a memorial to her husband, John W. Pepper, who died in 1918. Mrs. Pepper died, Dec. 23, 1934.

Pittsburgh

Travel Club Meeting.—The Obstetrical and Gynecological Travel Club, including physicians from Montreal, Boston, New York, Philadelphia, Chicago, Rochester (Minn.) and Washington, D. C., held its annual meeting in Pittsburgh, Dec. 2-4, 1934. Clinics were presented at various hospitals by the following Pittsburgh physicians: Drs. Charles H. Aufhammer, Charles J. Barone, Bender Z. Cashman, Sidney A. Chalfant, Josiah R. Eisaman, Thomas Evans Jr., Raymond A. D. Gillis, James L. Gilmore, Raleigh R. Huggins, David B. Ludwig, Thomas K. Reeves and Paul Titus. Among social features were a buffet supper at the home of Dr. Titus and a dinner at the University Club, at which Dr. Frederick C. Irving, Boston, read a paper on toxemias of pregnancy.

TENNESSEE

Bills Introduced.—H. 204, to amend the chiropractic practice act, proposes (1) that the membership of the board of chiropractic examiners be increased from three to five, (2) that the board be appointed by the governor from a list of names submitted by the Tennessee Chiropractic Association, and (3) to provide staggered terms of three years for board members. H. 265 and S. 168 propose, among other things, to impose an annual occupational tax on physicians equal to 1 per cent of the gross income derived from the practice of their profession.

Bill Enacted.—S. 97 has become a law, providing that the board of health shall consist of nine members, appointed by the governor, of whom six shall be licensed practitioners of medicine, one a licensed dentist, one a licensed pharmacist and one a member of the Tennessee congress of parents and teachers and the Tennessee Federation of Women's Clubs. The medical members are to be appointed from a list of names submitted by the Tennessee State Medical Association. The board is to formulate the policies and supervise the activities of the department of public health.

TEXAS

Bills Introduced.—S. 59 and H. 107 propose to authorize the sexual sterilization of mentally defective, deficient or diseased inmates of state institutions.

Gastro-Enterologists Organize.—The Texas Society of Gastro-Enterologists was organized, Nov. 16, 1934, during the meeting of the Southern Medical Association in San Antonio. Dr. Harry G. Walcott, Dallas, was elected president and Dr. Franklin D. Garrett, El Paso, secretary. The next meeting will be in connection with the annual session of the Texas State Medical Association in Dallas in May.

UTAH

Bill Introduced.—H. 4, to amend the workmen's compensation act, among other things proposes to make compensable any "disease which is the result of the occupation or employment."

WASHINGTON

Bills Introduced.—S. 14 proposes to authorize the establishment of a hospital for the treatment of drug addicts and to provide a procedure for the commitment of drug addicts to it. The bill defines a "drug addict" as one "who unlawfully administers to himself or unlawfully has administered to himself by others, any habit-forming narcotic drug." S. 32 proposes to eliminate from the criminal code those provisions prohibiting the possession, sale or other distribution, or the use, of contraceptives. H. 28 proposes to accord to physicians, nurses and hospitals, treating persons injured through the negligence of others, liens on all rights of action, claims, judgments, compromises or settlements accruing to the injured persons by reason of their injuries.

WISCONSIN

Bill Introduced.—A. 70 proposes to require every physician or midwife attending a confinement case to instil a 1 per cent solution of silver nitrate into the eyes of the baby immediately after its birth.

Two Positions for Women Physicians.—The state bureau of personnel announces that two vacancies are anticipated in the state board of health, for which women physicians are invited to apply: supervisor of the maternity and child welfare division, a permanent position, and maternity and child welfare physician, a position that will last about ten months, during a leave of absence of the present incumbent. Minimum qualifications are training equivalent to that represented by graduation from a medical school of recognized standing, a license or eligibility for a license to practice in Wisconsin, five years of practice with special experience in pediatrics and public health, ability as a public speaker, endurance, and good physical condition. Out of state candidates who are citizens of the United States will be accepted for both positions. Photographs and medical certificates must accompany applications, which must be filed before February 15. Blanks may be obtained from the bureau of personnel, Madison.

WYOMING

Bill Introduced.—S. 47 proposes to authorize any school district to employ a licensed physician to care for and treat school children.

GENERAL

License Missing.—Dr. Lewis Robert Wolberg, Kings Park, Long Island, N. Y., recently reported to the California State Board of Medical Examiners the disappearance of his license to practice medicine in California.

Association Favors New Food and Drug Legislation.—The American Association for the Advancement of Science at its meeting in Pittsburgh, Dec. 31, 1934, adopted a resolution supporting revision of the Food and Drugs Act. The statement expressed the conviction that cosmetics should be included in any new bill presented and that manufacturers, their salesmen or other agents, should be allowed to use in their advertising, printed, broadcast or otherwise presented, only such statements as are not misleading and are essentially in accordance with fact.

Orthopedists Form Examining Board.—At the annual session of the American Academy of Orthopedic Surgeons in New York, January 15-17, the American Board of Orthopedic Surgeons was organized to certify qualifications of physicians who wish to specialize in that field. Dr. Melvin S. Henderson, Rochester, Minn., was named chairman, and other members include Drs. Fremont A. Chandler, Edwin W. Ryerson and Philip Lewin, Chicago; Henry W. Meyerding, Rochester, Minn.; William Barnett Owen, Louisville, Ky.; John C. Wilson, Los Angeles; Hulett J. Wyckoff, Seattle, and Samuel Kleinberg, New York. Dr. Henderson was also chosen president elect of the academy and Dr. Frank D. Dickson, Kansas City, Mo., was installed as president. Dr. Lionel D. Prince, San Francisco, was elected vice president and Dr. Philip Lewin, Chicago, reelected secretary.

Lea and Febiger Publish Memorial Volume.—In recognition of 150 years of publishing, Lea and Febiger have just made available a sketch originally prepared by Mr. Henry Charles Lea in 1885 to celebrate the one hundredth anniversary of the founding of that business, revised and amplified to bring it up to date. The volume is beautifully illustrated with facsimiles of letters and with some fine portraits. This company has been operated continuously by members of the same family. The first editor of the *Philadelphia Journal of the Medical and Physical Sciences*, established in 1820, later the *American Journal of the Medical Sciences*, was Nathaniel Chapman, also first president of the American Medical Association. The publication became the *American Journal of the Medical Sciences* in 1827, under the editorship of Dr. Isaac Hays, who was also in charge of the committee that prepared the Principles of Ethics of the American Medical Association. The company takes particular pride in its continuous publication in America of Gray's Anatomy, beginning with 1859.

Annual Report of Commonwealth Fund.—Fifty-eight per cent of the $1,720,514.54 expended by the Commonwealth Fund in the year ended Sept. 30, 1934, was devoted to public health, rural hospitals, medical education and medical research, according to the annual report issued January 14. During the year the fund helped to finance a community hospital in Kingsport, Tenn., in the region served by the Tennessee Valley Authority, similar to the six community hospitals it has supported in the past few years. In the latter hospitals, average occupancy increased 22 per cent over the previous year and collections on patients' accounts increased 33 per cent. The fund has aided rural health agencies in Massachusetts, Mississippi and Tennessee. In Mississippi a special epidemiologic unit has been in operation. During the past few years 272 scholarships for graduate medical work have been given to physicians.

The fund is now subsidizing experiments at the Boston Children's Hospital and the New York Babies Hospital, in which students of pediatrics may observe psychiatric and psychologic methods of handling children. Support of the Child Guidance Clinic in London is being continued. Medical research sponsored by this foundation included a study of tuberculosis in the infant and preschool child at Johns Hopkins University School of Medicine, of placental extract at Harvard Medical School, and of serum treatment of pneumonia under the direction of the Massachusetts State Department of Health.

Medical Bills in Congress.—*Changes in Status:* S. 1226 has passed the Senate, proposing to prohibit the sending of unsolicited merchandise through the mails. S. 1175 has passed the Senate and House, extending the functions of the Reconstruction Finance Corporation for two years. The House rejected an amendment that would have authorized loans to colleges, universities and institutions of learning, and to hospitals. *Bills Introduced:* S. 337, introduced by Senator Vandenberg, Michigan, proposes to furnish to certain seamen hospitalization and medical treatment at hospitals and relief stations of the United States Public Health Service. S. 1375, introduced by Senator Copeland, New York, proposes to amend the penal laws of the United States so as to authorize the importation into the United States, and the interstate transmission by any express company or other common carrier, of books or information relating to the prevention of conception, or articles, instruments, substances, drugs, medicines, or things designed, adapted, or intended solely for the prevention of conception, if (1) for use by any physician legally licensed to practice medicine, or by his direction or prescription; (2) for use by any druggist in filling any prescription of any such licensed physician; (3) for use by any medical college legally chartered under the laws of the United States or of any state or territory, or of the District of Columbia; or (4) for use by any hospital or clinic chartered under the laws of the United States, or licensed under the laws of any state or of any territory, or of the District of Columbia. H. J. Res. 8, introduced by Representative Bland, Virginia, would authorize Hugh S. Cumming, Surgeon General, John D. Long, Medical Director, and Clifford R. Eskey, surgeon, all of the United States Public Health Service, to accept certain decorations bestowed on them by the governments of Ecuador, Chile and Cuba. H. R. 25, introduced by Representative Huddleston, Alabama, proposes to authorize the Bureau of Standards to adopt and prescribe grades and standards of quality of objects of commerce and to adopt and prescribe marks and symbols and/or figures indicating such grades and standards, and to adopt regulations for the use of such marks, symbols and figures as indicating quality, grade or standard. H. R. 2061, introduced (by request) by Representative Knutson, Minnesota, proposes to revise the laws and regulations relating to pensions and other allowances for veterans and their dependents. H. R. 3039, introduced by Representative McSwain, South Carolina, proposes to authorize the acquisition of additional land for the use of the Walter Reed General Hospital. H. R. 4317, introduced (by request) by Representative Zioncheck, Washington, proposes to incorporate the American White Cross Association on Drug Addiction. H. R. 4513, introduced by Representative Kopplemann, Connecticut, proposes to authorize the payment of claims for unauthorized emergency treatment of World War veterans. H. R. 4871, introduced by Representative Pearson, Tennessee, proposes to authorize the Reconstruction Finance Corporation to make loans to institutions of learning, and to hospitals. H. R. 5055, introduced by Representative Dockweiler, California, proposes to provide for the rehabilitation of, and uniform pensions for, all totally blind soldiers of the Army, Navy and Marine Corps, and war nurses.

Government Services

Progress in Testing of Cattle

Testing of cattle for tuberculosis is progressing more rapidly than at any time in the history of tuberculosis eradication, according to a statement from A. E. Wight, in charge of eradication of tuberculosis and Bang's disease for the U. S. Department of Agriculture. During November 1934 a total of 2,122,035 cattle were tested, more than in any month in the history of the nation wide campaign. Although the work against Bang's disease is more recent, reports from forty-four states show that more than 286,000 agglutination tests were made in November. Nearly 15 per cent of the cattle reacted and will be removed for slaughter. Large numbers of cattle are on the waiting list for examination. This work is financed by federal and state funds from various sources, with impetus from funds provided by the Agricultural Adjustment Administration.

Internship Available at St. Elizabeth's

The U. S. Civil Service Commission has announced a competitive examination for junior medical officer (intern) at St. Elizabeth's Hospital, Washington, D. C., for which applications must be on file not later than February 18. Two types of internship are offered. The first type is a two year internship consisting of a rotating service of four months each of surgery, acute medical service and chronic medical service; six weeks each of obstetrics and pediatrics (affiliation); three months of general laboratory work, and six months of psychiatry. The second type is a graduate internship of one year in psychiatry, for which physicians who have already had an accredited internship are desired, although applications will be accepted from those who have not. Applications will be accepted from fourth year students in medical schools that require a year of internship before granting a degree, as senior students to serve the intern year, and from senior students in other schools subject to their furnishing proof of graduation during the existence of the eligible register. Full information may be obtained from the secretary of the U. S. Civil Service Board at the postoffice or customhouse in any city that has a postoffice of the first or second class or from the Civil Service Commission, Washington, D. C.

Annual Report on Health of Army

For the first time in the U. S. Army, injuries from athletics lead the causes of admission to sick report with a rate of 28.4 per thousand, according to the annual report of the surgeon general for 1933. The lowest admission rate (578.5) ever achieved was recorded for this year, while a new low rate (34.4 per thousand) was indicated for venereal disease incidence as compared with 42 for the previous year. The total army had an average daily strength of 136,491 during the year, an increase of 4,566 over that of the previous year. The percentage of first enlistments of the total number enlisted was 38.2, which was higher than the two previous years (25.5 and 29.8), but lower than the rate of 43.6 for 1930. The total number of days spent in the hospital during the year was 1,355,245. In addition there were 1,008,140 hospital days chargeable to beneficiaries of the Veterans' Administration, soldiers' homes, members of the national guard, officers' reserve corps, reserve officers' training corps, citizens military training camps, civilian conservation corps and civilians entitled to medical treatment. This totals 2,363,385 hospital days as compared with a total of 2,425,343 days spent in hospital during 1932. In addition there was an average of 395 patients each day treated in quarters and 1,290,142 outpatients treated. There were 686,327 physical examinations performed and 949,966 vaccinations of various kinds administered. For the fiscal year 1934 the per diem cost of hospitalization in army hospitals was $4.60. The number of Veterans' Administration beneficiaries was materially reduced, but this was offset by the influx of civilian conservation corps patients. The admission rate for officers (487) was the lowest for the past decade. There were 577 deaths during 1933, as compared with 567 in 1932 and 626 during 1931. Excluding three of these deaths, which were among nurses, the death rate for the whole army was 4.2 per thousand, as compared with 4.3 the previous year. Automobile accidents headed the list as the most important cause of death, as they have since 1930. During 1933 there were seven more than in 1932 but twelve less than in 1931. Collisions with other vehicles accounted for eighteen of the eighty deaths from this cause. Suicides stood second as a cause of death, accounting for fifty-seven deaths; airplanes, responsible for fifty-six deaths, were third. Deaths from external causes gave a rate of 2.10, almost as high as the total rate for diseases, 2.11. During the year ninety-two officers and 1,721 enlisted men were discharged from the service on account of physical or mental disability, a total of 1,813, as compared with 1,566 for 1932. The rate of discharge for the year for the entire army was 13.3. The noneffective rate for the whole army for the year was 29.4, as compared with 30.5 for 1932 and 32.5 for 1931. Gonorrhea was the leading cause for the loss of time, 2,863 cases accounting for 133,531 days lost. However, tuberculosis led the conditions causing the greatest loss of time per case, on account of the long continued treatment required. Injuries caused 19.7 per cent of all noneffectiveness, as compared with 18.8 for 1932. The rate 5.6 was the lowest on record for alcoholism for the total army with the exception of the war years. Twelve drug addicts were detected, as compared with sixteen in 1932.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Jan. 12, 1935.

The State Assistance of the Unemployed

Following the war the unprecedented unemployment led to equally unprecedented government expenditure for its relief, and controversy arose as to the amount of food necessary for the maintenance of health and its cost. The question was at first scientific but it quickly became political, for, whatever was given, the labor party demanded more. In the house of commons, Mr. Oliver Stanley introduced for the government a draft of unemployment assistance regulations. He said that the scales proposed were the result of a careful survey by the Unemployment Assistance Board of the primary needs of the people for whom the board was responsible. There were great differences in the results arrived at by different social surveys. In the spring of 1934 a hotly contested debate took place in the house of commons as to whether the allowance for a child should be 48 or 72 cents a week. (This does not mean that parents were expected to keep children on this expenditure but merely that it is an allowance per child to persons with other resources such as the unemployment dole.) In the new scale the minimum allowance for any child is 72 cents and that amount increases with age, which is a new principle. Dealing with the question of the treatment of resources other than earnings in assessing needs, the basis to be adopted with regard to milk and meals given to children at schools is as follows: All meals given on a physician's certificate that a child is suffering from a specific condition and requires extra nourishment are to be regarded as personal medical requirements and ignored. Milk or other special items, such as cod liver oil, will also be entirely ignored. Meals up to two a day for a single child in a household or one meal for two children will be ignored as constituting a negligible saving for the family. That is to say, twelve meals a week will be free. After that some deduction will be made in respect of those meals, which works out roughly at two cents a meal. As regards medical relief, maternity and child welfare, and tuberculosis services, any payments or allowances in kind under these services will be regarded as special needs and will be ignored. In the case of pensions for old age, widows and orphans and the blind, any balance after providing for the pensioner's needs would be allowed for the personal needs when there were no other resources; that is, they would be ignored. In the debate that followed, a physician, Sir Francis Freemantle (a retired health officer), described the new regulations as a great measure, but they were opposed by the labor party as inadequate. They were carried by a large majority.

An organization called "The Children's Minimum Committee," formed to ensure the adequate nutrition of children, welcomes the new regulations as a considerable advance but points out that for families with two or more children the proposed scale will not permit of an expenditure satisfying the standards laid down by the British Medical Association's Committee on Nutrition. The Children's Minimum Committee urges that the scale should be supplemented by free meals and milk, which should not be taken into account in assessing the family resources.

The Prevention of Mule Spinners' Cancer

The Manchester Committee on Cancer, formed in 1925, is representative of all the hospitals and public health authorities in the city. Its major work has been the establishment of a laboratory unit in the university, primarily for investigating the causes and prevention of mule spinners' cancer, so alarmingly prevalent in the cotton mills of Manchester and the neighboring towns. Increasing incidence of mule spinners' cancer began to be noticed about 1908. This led to the appointment by the government of a special committee of investigation. In 1926 it was reported that the death rate from this form of cancer in cotton operatives was 137 for spinners and 72 for other cotton workers, while the mean national death rate was 4 per million living males. It was found that spinners' cancer was due in part, if not entirely, to mineral oil. The Manchester committee therefore undertook an investigation as to the possibility of purifying the mineral oils likely to cause cancer. Their scientists were the first to examine this problem from the special point of view of cotton mills. The results have now reached a practical stage. The amount of work done by pathologists, chemists and physicists in the investigation during the nine years is enormous.

As reported previously (THE JOURNAL, Dec. 22, 1934, p. 1959), the director of the Cancer Research Laboratories, Dr. C. C. Twort, has been able to lay down a specification for lubricating oils that should reduce the risk of cancer to a minimum. The precancerous conditions of the skin due to handling mineral oils are now being almost altogether prevented by the precautionary measures recommended. These observations constitute the first real preventive work in cancer that has been effected in this country and, so far as is known, in the world. A similar line of investigation is now being carried out in relation to tar compounds and concern gas-tar workers, distillers, tarmac road workers, and others. Considerable evidence has been collected to show that the increasing incidence of cancer of the lung is associated with contamination of the atmosphere by smoke. The action of the exhaust fumes of automobiles is also under investigation.

Some mineral oils were found to be more carcinogenic than others, but all, other than white oils (such as medicinal liquid petrolatum and the lighter boiling spirits), were potentially carcinogenic. Textile oils were the most carcinogenic, considerably more than the heavier internal combustion engine oils. The animal test of carcinogenicity is lengthy, laborious and expensive. To avoid these difficulties the chemical and physical characters of the oils were investigated and the results proved to be of the greatest utility, allowing oils to be condemned or recommended. The refractive index and the specific gravity were the test of greatest value and allowed animal tests to be dispensed with entirely. As a prophylactic against industrial cancers, an ointment composed of equal parts of wool fat and olive oil gave the greatest protection. It is recommended that all parts of the body likely to come in contact with the suspected material should be smeared with this before work is begun. After work the parts should be washed with soap and water and carefully dried, a little of the ointment being again rubbed in.

The Laboratory and the Clinic

In his presidential address to the Royal Society, Sir F. Gowland Hopkins said that practice in the ward and activity in the laboratory, which only a generation ago made few contacts, have now come into close relations, with a degree of mutual respect between their respective workers that was perhaps lacking in the past. It seemed that the minds of some physicians have been disturbed by one aspect of this new orientation. Not doubting that the laboratory has assisted, and must continue to assist, the growth of medical knowledge, they have felt that the introduction of multitudinous laboratory methods into the domain of diagnosis is tending to destroy the true clinical art. It had been said that the older physicians with minds undisturbed by a crowd of scientific facts developed a clinical sense, sui generis, as subtle as the sense of taste or the sense of smell, and that it was on this sense that the great school of English medicine was founded. The president did

not know whether there was truth in the view that reliance on laboratory reports tended to destroy this sense. Great emphasis was being laid on the fact that, distinct from all the laboratory science which was ancillary to medicine, there was a clinical science, the progress of which depended on the direct and intimate study of disease as manifested by human beings. The need had been expressed for the endowment of a phalanx of trained clinicians who shall bring clinical science to a new pitch of efficiency.

The Relation Between Stammering and Left-Handedness

At the annual Conference of Educational Associations, Dr. Millais Culpin, lecturer on psychoneuroses to the London Hospital Medical School, in introducing a discussion on speech therapy, spoke of the relation between stammering and left-handedness. In right-handed persons, he said, the left cerebral hemisphere was trained, but at the same time the right hemisphere was, one might say, acquiring knowledge in mirror fashion. If a man lost his right arm he tried to write with his left hand, and if he was allowed to write in mirror fashion he would do so in a very short time. In a child born left-handed stuttering resulted, according to the view of a famous anatomist, from conflicting control—ineffectual attempt to enunciate by reversal of the proper muscular action. This sounded simple, but there were objections to the theory. The same anatomists said that to a sensitive child the mental conflict that might arise from such causes might have serious consequences on the temper and character. What kind of person, however, was the left-handed? The left-handed had a peculiar make up. They were calm and deliberate; they demanded justice for themselves and others, and they showed a spirit of deliberate obstinacy. They did not get wild; they just calmly went on their own road. In the discussion which followed, Dr. E. J. Boone, director of speech therapy of the London County Council Schools, said that speech therapy was coming into its own and had come to stay. His own experience was that stammering was definitely curable.

PARIS

(From Our Regular Correspondent)

Dec. 27, 1934.

Foreign Physicians in France

According to de Lafond, the number of foreigners practicing medicine in France was 9.9 per cent of the total of 26,205 physicians in 1931. In the latter year, 28.2 per cent of the licenses in Paris were given to foreigners. There were only 429 medical students of foreign birth in 1920 and 1,511 in 1930 out of a total of 4,500 in the Paris medical school.

There are a number of ways to explain this plethora of foreigners. One is the reputation of the Paris school. Another is that the number of medical students has been greatly restricted by legislation in Brazil, the United States, Canada, Sweden and a number of other countries. A third reason is that many prizes and cheap living quarters in the Cité universitaire tempt the foreign student to come to France. Last of all, especially since the World War, France has become a harbor of safety for the refugees from all other countries, such as Russia and more recently Germany.

There will be a decided reduction in the number of medical students and hence of practitioners of foreign birth in the near future. A new law, termed the Armbruster law, abolishes permitting foreigners to be excused from any of the required work in the medical school. Heretofore they could be admitted to the fourth year and thus were obliged to pass the examinations only of this and the final or fifth year. In the future, the full six years in the medical school and a bachelor of arts degree from a French university will be required of every foreigner, the same as for any native student. Up to the present, Rumanian students have not been obliged to pass the French baccalaureate examinations. In 1933 more than 700, or about one sixth of the students, in the Paris medical school were Rumanian who had taken advantage of such a clause in a treaty between France and Rumania dating back to 1860.

No one will be permitted to practice medicine in France unless he bcomes naturalized. The only exception is that in the case of countries like the United States and England, which allow a French citizen to obtain a license without becoming naturalized, are exempt from this portion of the Armbruster law, which is now in effect. Of course, in about one third of the states in the case of the United States, an applicant for a license must agree to become a citizen. As a result of the Armbruster law, the number of American and English physicians in France will be greatly lessened and possibly may reach a negligible figure.

In the past, the medical schools have granted a diploma, termed "Diplôme universitaire," which did not carry with it the privilege to practice in France or its colonies. If as many foreigners continue to take the courses as in the past, there will be but little relief from the present overcrowding in the medical schools, even though the Armbruster law is in effect. Fortunately, the economic crisis existing in the majority of countries has begun to decrease the number of foreign students in France since 1931, at which period there were 17,281, while in 1934 there were only 14,495. That medical schools are stricter in granting diplomas is shown by the fact that, in 1931, 1,446 were given in a total of 7,336 medical students, while in 1933 there were 12,407 students in the medical schools but only 1,552 diplomas were bestowed.

Is Phrenic Resection Beneficial in Pulmonary Tuberculosis

In the Dec. 1, 1934, issue of the French medical gazette, the results of seventy-four phrenicectomies are reported by Delay, Colbert and Mollard. The three indications for the operation were, first, those cases of pulmonary tuberculosis in which a pneumothorax had not been followed by any improvement or was impossible because of pleural bands or adhesions. The second group included cases in which the resection of the phrenic nerve supplemented the pneumothorax. Later, and this forms the third group, the nerve resection was done primarily in preference to a pneumothorax, either because the latter appeared contraindicated by extensive bilateral lesions or because the lesions in the lung were still too recent.

No complications were observed in the seventy-four cases in which phrenicectomy was performed, such as gastric disturbances or lighting up of foci on the same or opposite side. In one third of the cases there was considerable pain during the operation, due to prolonged search for the nerve. There are also some cases in which one finds anomalies, such as that the nerve that was resected is found, after the operation, not to have contained any of the motor fibers for the diaphragm.

As to the results of the seventy-four operations, thirty-one patients were markedly and eleven only slightly (symptomatically) improved. Thirty-two cases failed to show any benefit from the nerve resection. In the thirty-one in which there was marked improvement the lesions in the immobilized lung had diminished in size and the clinical symptoms had disappeared completely. None of these thirty-one cases had shown previously any improvement after prolonged sanatorium treatment. Eight of the thirty-one can be considered as completely recovered. The less active the lesions, the greater is the chance of success after phrenicectomy. If the lesions occupy half or two thirds of a lung, the operation is of no avail. Phrenicectomy is especially useful for lesions of the base, hilus or central regions of the lung. The nerve should be resected for a distance of 7 or 8 cm.

BERLIN

(From Our Regular Correspondent)

Dec. 3, 1934.

Research on Leukemia

Since the essential nature of leukemia has appeared to be less in the increase in the leukocytes than in the tumor-like proliferations of the blood-forming organs, leukemia has been classified with the malignant tumors by some investigators. Leukemia has been considered a true tumor of the hematopoietic tissue, usually accompanied by a flooding of the blood stream with a large number of immature cells. Objections have been made to the interpretation of leukemia as a tumorous condition, but no agreement has been reached. Dr. Walter Büngeler of the pathologic institute in Danzig has attempted to produce experimentally in mammals, leukemia, aleukemic myelosis, lymphadenosis and lymphosarcoma. Büngeler was able to demonstrate that the development of leukemia takes place according to the same laws as do malignant tumors, and, moreover, that the tissue metabolism of leukemic proliferations differs in no respect from the tissue metabolism of malignant growths.

Disturbances in embryonal development are the first factors in the etiology of leukemia, and this is the case also in malignant growths; congenital leukemias have been described repeatedly. Then there are studies based on the regeneration theory. Fischer-Wasels in Frankfort-on-Main as well as Büngeler demonstrated that regenerative processes, which under normal conditions lead without exception to complete restoration, frequently become the seat of a tumor formation, if in the experimental animals a predisposition has been produced by the prolonged administration of tar or arsenic. This predisposition can be recognized by certain changes of the metabolism. The parenteral administration of indole produces similar metabolic changes as those resulting from the administration of tar and arsenic. In studies on indole, Büngeler observed peculiar organic changes on the hematopoietic tissue. A large number of the white mice die within the first eight weeks with the signs of poisoning, if they are subjected to intensive indole treatment; in others, hemolytic anemias developed accompanied by a reduction in the leukocytes and by hemorrhages and necroses in the bone marrow, in the spleen or in the liver. During the eighth month of the indole treatment, tumor-like proliferations of the hematopoietic organs develop in a large percentage of the animals. Apparently it depends on constitutional factors whether, under the influence of the same treatment, one group of animals develops a tumor of the lymphatic tissues or a tumor of the myeloid tissue. However, the observation that the same experiments may result in leukemia or in lymphosarcoma justifies the conclusion that the two conditions are closely related. These experiments prove that leukemias, like other malignant tumors, may develop on the basis of regenerative processes. Accordingly the pathogenesis of this fatal disease is governed by the same laws as is that of other malignant tumors. Moreover, the leukemic proliferations have a metabolism which, with its greatly increased fermentation, resembles in all respects that of malignant growths. Büngeler concludes that leukemia is a malignant growth of the blood-forming apparatus. Lignac recently arrived at the same results by means of chronic poisoning with benzene. Indole is a compound that develops in the course of intestinal putrefaction. These studies are carried on with the support of the Lady-Tata Memorial Foundation.

Silicic Acid in Blood of Patients with Silicosis

In the Kaiser Wilhelm Institute in Dortmund and Münster (Westphalia), experiments on silicosis have been conducted for some time. They were discussed in THE JOURNAL, Feb. 10, 1934, page 471. Prof. Heinrich Kraut determined previously that the silicic acid content of the blood of normal persons amounts to from 1 to 3 per cent of the ash. The average value of the silicic anhydride in the blood ash of sixty persons was 1.8 per cent. The limits were 1.5 and 2.1 per cent, respectively. Tests on seventy-nine patients with silicosis revealed that their blood ash nearly always had high silicic acid values, on the average 3.5 per cent of silicic anhydride. The values fluctuated between 2.4 and 4.5 per cent. Patients with silicosis thus have an increased silicic acid content of the blood; that is, dissolved silicic anhydride has been absorbed by the organism. To determine the length of time a miner works on rock formations containing silicic acid before these chemical influences on the organism become manifest, the blood of 265 miners was tested for the silicic acid content in connection with the roentgenologic examination, to which they were subjected at regular intervals. The blood ash of these workers has about the same average silicic anhydride content as has that of other persons, namely, 1.9 per cent; but the upper and the lower limits are considerably farther apart (3.1 and 1 per cent). In workers without demonstrable silicotic changes, the upper and lower limits of the silicic acid content move farther apart within the first six years of time they have worked on silica rock, and in the following twelve years the movement is primarily upward. In workers who develop a slight silicosis within the first six years, without becoming incapacitated, a great increase becomes noticeable, up to 3.8 per cent of silicic anhydride. In the two subsequent six-year periods, this increase partly subsides again, doubtless because men with high silicic acid content of the blood are eliminated from the group, because of severe silicosis. This is indicated not only by the comparison with the values of those silicosis patients no longer able to work but also by the results of the examinations of miners who have worked on silica rock more than eighteen years, in whom the values closely approach once more the upper and lower limits in normal persons. This is the case particularly in workers without signs of silicosis and also in those who already have a slight silicosis. The wide fluctuations prevent as yet the elimination of those who are in danger on the basis of the abnormal silicic acid values of their blood.

The Psychiatric Examination of van der Lubbe

Professor Bonhoefer, director of the psychiatric clinic of the University of Berlin, and his assistant Dr. Zutt, have published the testimony they rendered in the case of M. van der Lubbe, the incendiary of the Reichstag fire. They stress that, on the basis of the public trial, it was impossible to get a clear picture of van der Lubbe's mental condition, and this fact has favored the spread of phantastic rumors. For persons with psychiatric training it would have been unnecessary to refute the explanation that the behavior of the defendant was due to hypnosis and the administration of scopolamine; nevertheless, they examine these charges briefly and call attention to the absence of dilatation of the pupils and of all signs of a narcotic or hypnotic condition. The scientific value of the neuropsychiatric examination would have been greater in case of a conclusive solution of the case, which was not accomplished. But even with this limitation the psychiatric testimony is of interest. While the authors deny the existence of a disturbance of the consciousness when the deed was committed, this does not prove that van der Lubbe was normal. They consider him a psychopath who has to be considered accountable for his actions. His mutistic behavior during the trial is interpreted as a spite reaction. It was not an intentionally assumed attitude but rather a psychogenic-reactive state that can be compared to the obstinacy stupors of children. The outburst on the forty-second day of the trial, on which van der Lubbe talked for the first time of inner voices, was no surprise to the psychiatrists. It is interpreted as the expression of a prison reaction. However, the attitude of the defendant during the entire duration of the imprisonment, the affective inexorability and the consequent

moroseness, is an astounding performance, which is understandable when it is considered that van der Lubbe was an extraordinary person. According to the psychiatrists, he was a confused fanatic with a mixture of craving for applause and self sacrifice, good-natured responsiveness and an attitude of defiance. His average intelligence was not equal to his essentially mental interests, but in spite of this he showed an astounding determination by steadfastly refusing to identify the accomplices he may have had. The expert in matters of arson questioned the statements of van der Lubbe, and that may have been a contributory cause in the outburst on the forty-second day of the trial. The two psychiatrists reach the conclusion that the psychopathically predisposed defendant cannot be considered mentally diseased.

VIENNA

(From Our Regular Correspondent)

Dec. 10, 1934.

The Birth and Death Rates

The federal ministry for public health recently published a summary of the status of the population of Austria of the last few years. The decrease in the birth rate has advanced further. Compared with the preceding year the numbers were as follows:

	1932	1933
Total number of births	105,514	98,861
Total number of deaths	93,721	89,071
Excess of births	11,793	9,790

Thus the excess of births was reduced by 2,000. If one looks back twenty years, the falling birth rate is even more evident. There were born in the region of present-day Austria and in Vienna:

	In Region of Present-Day Austria	In Vienna
1913	169,060	39,155
1923	155,704	29,691
1933	98,861	13,746

That reveals for Austria a reduction in births of more than 70,000, or 40 per cent, and for Vienna alone more than 66 per cent (26,000) in twenty years. Whereas in Vienna the status of the population is kept at the same level only by immigration from the provinces—the death rate far exceeds the birth rate—there is still a slight excess of births in the provinces; but this will probably disappear within the next ten years if there is no noticeable change in the mortality. Ten years ago (1923) the number of deaths in Austria per thousand inhabitants was 15.3, the births 22.5; that is, there was an excess of births amounting to 7.2. In 1933, however, the death rate was 13.6, the births only 15.1, an excess of 1.5, which doubtless will soon disappear. For Vienna, the figures are:

	1923	1933
born per thousand inhabitants	15.9	7.3
deaths per thousand inhabitants	13.7	13.6

that is, an excess of deaths over births of more than 6 per thousand inhabitants. The mortality is constantly decreasing. There is a shifting of the average age at death into the higher age groups. The population becomes older, as shown in the following tabulation of 1,000 deaths, as to the age group:

	1923	1932	1933
0 to 5 years	246	149	128
5 to 15 years	29	26	26
15 to 30 years	80	63	60
30 to 50 years	132	137	131
50 to 70 years	266	310	317
Over 70 years	246	324	338

The death rate of nurslings is likewise constantly decreasing. Of 1,000 live births there died during the first year of life

	1923	1932	1933
In Vienna	110	75	64
In Austria	140	106	94

The mortality rate of nurslings is satisfactory, since it is constantly decreasing. However, the growing reduction in the birth rate, as demonstrated above, is to be deplored. There is still a constant number (above 4 per cent) of births that take place without trained helpers. This is explained by the considerable number of women who live in forests and in the mountains. The number of stillbirths likewise is about constant, on the average 2.5 per cent during the last ten years. The number of illegitimate births likewise remains about the same, about 26 per cent.

As regards the causes of death, the diseases of the heart and of the circulatory system take the first place, 15,966; then follow malignant tumors, 11,249; then tuberculosis in all its forms, 8,086; then pneumonia, 7,383; then apoplexy, 5,838. Infectious diseases (with the exception of children's diseases) caused 1,590 deaths; wound infections, 1,370; fatal injuries due to accidents caused 2,287 deaths; the number of suicides was 2,853 and the homicides 198. Only 244 women died of puerperal sepsis. This number is rather small when it is considered that over 4,000 births take place without assistance. During the last five years there was not a single fatality due to smallpox, typhus and cholera, but diphtheria caused 990 fatalities, whooping cough 147, scarlet fever 124 and measles 89 (compared to 300 in the previous year). On the whole, the children's diseases caused a much greater number of fatalities during the previous year. Cholera infantum caused 526 (compared to 813) Abdominal typhoid caused 121 fatalities and dysentery 21. The reports of recent years show with increasing clarity that the mortality rate of cardiac and cerebral disorders steadily increases, relatively as well as absolutely. These two factors are now responsible for 20 per cent of all deaths, while twenty years ago they were responsible for only 12 per cent.

Investigation of Methods of Irradiation of Carcinomas

At a recent session of the Vienna Society for Roentgenology, Dr. A. Frank reported about his studies on the method of irradiation of large carcinomas consisting of pavement epithelium. Half of the carcinoma was irradiated with one large dose (1,800 roentgens), while the other half was daily irradiated with a so-called fractional dose consisting of 200 roentgens until a total of 4,000 roentgens had been reached. The quality of the rays and the roentgen minute dose were the same. By the time 1,000 roentgens had been administered to the side that was given the fractional irradiations, a considerable decrease in the size of the tumor was noticeable, while the side to which the single large dose had been applied showed no macroscopic signs of a change, in spite of the fact that the surrounding skin, which had been exposed to this radiation, reacted noticeably. When 1,800 roentgens had been reached, the same dose that the other side had had, the tumor had largely disappeared on the side irradiated with the small doses, while on the other side macroscopic changes were still lacking. In the further course it was observed that on the side to which the single, large dose had been applied the tumor was still partly in evidence, while it had completely disappeared on the side to which the fractional doses had been applied. Histologic studies revealed that on the side of the fractional irradiations the tumor cells were destroyed by undergoing cornification and maturation, while on the side of the large dose a vacuolizing degeneration took place. Studies conducted in several other suitable cases led to the same results. In view of these observations, Dr. Frank formulated the thesis that the application of a single large dose leads to a less rapid disappearance of a tumor than the fractional irradiations. This factor is important when the danger of metastasis is considered, for it has been assumed erroneously that in case of fractional irradiation the danger of metastasis is greater. In the discussion it was pointed out that the nature of the cells of the neoplasm as well as its reaction capacity to the x-rays is of great importance in the evaluation of a method of irradiation. However, many agreed that fractional irradiations are generally to be preferred.

Pictures of a Giant

Prof. D. H. Fuchs, who recently returned to Vienna from the Orient, showed at the last meeting of the Society of Physicians photographs of a giant, whom he had seen in Bushire, Persia. The giant was 10 feet 6 inches (3.2 meters) tall and was 19 years old. He had developed normally up to his tenth year, when he began to grow enormously. Mighty humps developed on his forehead, chin and behind the ears. The head became so heavy that the man could not hold it up. The humps on the forehead caused a great forward curvature. They have the appearance of tumors. There are many other lighter, loose nodules in the wrinkled skin. In the enormous head the eyes appear, in spite of their normal size, extremely small; the vision is good and the teeth are normal. The extremities are of an enormous length, the proximal phalanx being as long as the index finger of a normal man. The legs are too weak to enable him to walk, so he is generally lying down; but he is able to stand up when supported by a cane. His intelligence is almost normal; he complains frequently of vague pains. Recklinghausen's disease has been considered as the etiologic factor and it is assumed that an early localization of the process in the hypophysis or in the growth center is responsible for the giant growth. The patient was unable to ride in an ordinary carriage and he had to be placed on a boat by means of a crane. His weight exceeded 200 Kg. (450 pounds).

ROME

(From Our Regular Correspondent)

Dec. 31, 1934.

The Readjustment of Clinically Cured Tuberculous Patients

Dr. Alfonso Muzzarelli of the Consorzio Provinciale Antitubercolare of Florence reported the results of studies on readjustment to work of tuberculous patients who have been discharged from sanatoriums as "clinically cured." When these patients reenter work, they are confronted by demands beyond their physical conditions. It seems advisable therefore to establish postsanatorial colonies adjacent to the sanatoriums to prepare patients for work, while still under medical supervision. A temporary regimen for tuberculous patients in these colonies will result in the correction of lazy habits acquired during their long stay in the sanatoriums. It will also open up new fields of work when the work previously done has to be changed more in accordance with the type of cure obtained in the given case.

Prizes in Ophthalmology

The Società Italiana di oculistica has reviewed the most important articles presented in the annual competition for ophthalmologic prizes. The awards were as follows: The national prize, 20,000 lire (about $1,400), to Dr. Parnico of Rome for an article on biomicroscopy of the palpebral margins, and of conjunctivitis. The first international prize, 20,000 lire, to Dr. Benedetto Strampelli for an article on biomicroscopy and histology of cataract with polarized light. The second international prize to Dr. Nordmann of Strasbourg for his physicochemical studies of the crystalline lens in normal and pathologic conditions.

The National Congress of Pediatrics

The fifteenth National Congress of Pediatrics was held at Sienna, with a large attendance from Italy and abroad. The first topic was "Sepsis in New-Born Infants and Nurslings." Dr. Bocchini said that sepsis causes symptoms of a grave general infection that overshadow those of the first focus of infection. The predisposition to the development of sepsis in infants is related to their conditions of immunity. A passive but transient immunity is acquired from the mother, which protects them against diseases to which the mother herself is immune. This defense mechanism in infants is built up by organic processes of slow evolution and may be weak against pyogenic infections because of minimal cellular reactions and the scant activity of the phagocytes. Breast feeding provides the child with the proper nutrition whereby the organism can promptly meet the immunologic demands. Artificial feeding may cause nutritional disturbances that result in a lowering of the defense against infections. A diminished amount of vitamins in the milk, environmental conditions, and the existence of some constitutional diathesis are the most important factors in the onset of septic infections.

Dr. Gerbasi discussed the pathology, blood picture, diagnosis, prognosis, prevention and treatment of sepsis. The most important changes are in the liver, respiratory tract, adrenals and bones of the skull. The blood picture is not definite and it has a prognostic value only when it is within certain limits. Immature erythrocytes and leukocytes frequently appear in the blood, simulating the picture of anemia of the Jaksch-Hayem type. The roentgen examination of skeletal foci gives diagnostic results as satisfactory as those given by the bacteriologic examination of the blood. Prevention depends largely on the care of infants and their environment. The attempts at immunization in the prevention and therapy of sepsis have not given satisfactory results as yet.

Dr. Vaglio said that attenuated forms of sepsis are difficult to diagnose and may be mistaken for nutritional disturbances, prematurity and congenital weakness. Sepsis may be of the hyperacute, acute or attenuated form. Symptoms similar to those observed in sepsis may be observed also in diphtheria, alimentary toxicosis, malaria, tuberculosis and congenital syphilis. The members of the congress voted to recommend a revision of the projects concerned with the construction of pediatric institutions, special training for the personnel concerned with the care of infants, and the provision of sterilized linen for them.

The second topic was "Indications for Climatotherapy for Infants." Dr. Bentivoglio classified climates into stimulative, sedative and indifferent, and insisted on the importance of establishing a classification for each climatic station.

Dr. Magni spoke on the indications for the sojourn of children at the seashore. He concluded that the climate at the seashore is a powerful agent for the prevention and treatment of certain infantile diseases, especially certain forms of external tuberculosis, rickets and peribronchial adenopathies.

The third topic was "The Sympathetic Nervous System in Infants." Dr. Careddu said that this subject should be considered, as yet, a program to be developed rather than as an exposition of results already acquired. He discussed the evolution of the sympathetic cells, which need several years during the first two decades of life to reach their complete development and definite adjustment. The main function of the sympathetic nervous system is the regulation of the internal equilibrium of the body by means of rhythmic sympathetic, visceral, motor and sensory reflexes. The parasympathetic energies predominate during childhood in order to provide a greater activity to the anabolic processes.

Dr. Guassardo said that the physiology and pathology of infants are chiefly controlled by the vagus nerve, the preponderance of which determines an exaggerated reaction of the body to even slight stimulations, which may result in disturbing the normal sympathetic equilibrium necessary for the conservation of health. The development of diseases in infants depends on the constitutional tendency, and that statement applies especially to such diseases as exudative diathesis, spasmophilia, anaphylaxis, and cyclic vomiting. That is why the conception of the existence of a hypervagal sympathetic diathesis establishes a bridge connecting the pathology of the parents with the future morbid predisposition of the children.

The next national pediatric congress will meet at Genoa.

Marriages

CHARLES LEE ANDERSON to Miss Frances Elizabeth Behnes, both of Jackson Heights, N. Y., Dec. 21, 1934.

WILLIAM JOHN MACKENZIE to Miss Enid Howell, both of Vancouver, B. C., Canada, Dec. 15, 1934.

JACOB MOSCOVICH to Miss Mary Armstrong, both of Vancouver, B. C., Canada, Nov. 30, 1934.

MOSES KAHN ROSENBAUM, Milwaukee, to Miss Pearl Finnegan, in Chicago, Dec. 22, 1934.

SAMUEL E. KOHN, Milwaukee, to Miss Rita Jane Goldman of Whitefish Bay, January 10.

THOMAS HARDGROVE to Miss Evelyn O'Leary, both of Milwaukee, Dec. 29, 1934.

LAWRENCE M. CALDWELL, Newton, N. C., to Miss Macel Ratchford, January 4.

BENJAMIN POLOW to Miss Buddy Wachstein, both of Newark, N. J., January 23.

MONTE SALVIN to Miss Joyce-Tichnor, both of Los Angeles, January 26.

Deaths

Clarence Pierson ● Pineville, La.; Tulane University of Louisiana Medical Department, New Orleans, 1894; member of the House of Delegates of the American Medical Association, 1919-1920; past president, and formerly councilor of the sixth district, Louisiana State Medical Society; member of the American Psychiatric Association; past president of the Louisiana Hospital Association; veteran of the Spanish-American War; parish coroner, 1896-1900; at one time bank president; formerly medical superintendent of the Central Louisiana State Hospital, Pineville, and the East Louisiana State Hospital, Jackson; special consultant to the three eleemosynary institutions for the insane and feebleminded, Central Louisiana State Hospital, Pineville, East Louisiana State Hospital, Jackson, and the State Colony and Training School, Alexandria; aged 66; died, Dec. 27, 1934, in the Touro Infirmary, New Orleans, of carcinoma of the stomach.

Alfred Owre, Pine Plains, N. Y.; Minneapolis College of Physicians and Surgeons, 1895; also a dentist; dean and professor of dentistry, School of Dental and Oral Surgery, Columbia University, 1927-1934; student assistant in operative dentistry, 1893-1894, instructor in dental metallurgy, 1895-1896, instructor in operative dentistry and dental metallurgy, 1896-1897, clinical professor of operative dentistry in 1899 and dean and professor of theory and practice, 1905-1927, College of Dentistry, University of Minnesota; member of various international dental congresses; past president of the Minnesota Dental Association; special consultant in dentistry, Presbyterian Hospital, New York; aged 64; died, January 2, in the Beth Israel Hospital, New York.

Gaston Holcombe Edwards ● Orlando, Fla.; Yale University School of Medicine, New Haven, 1902; member of the House of Delegates of the American Medical Association in 1925 and in 1931; fellow of the American College of Surgeons; councilor of the seventeenth district and past president of the Florida Medical Association, Florida Railway Surgeons' Association and the Orange County Medical Society; aged 59; consulting gynecologist and obstetrician to the Florida Sanitarium and Hospital and chief of staff, department of gynecology and obstetrics at the Orange General Hospital, where he died, Dec. 29, 1934, of heart disease.

Leonard Samuel Hughes ● Lieut. Colonel, U. S. Army, retired, Los Angeles; Louisville (Ky.) Medical College, 1897; a contract surgeon from 1898 to 1908 when he was commissioned in the medical reserve corps as a first lieutenant and served in this capacity until 1911, when he was appointed first lieutenant in the medical corps; promoted to major in 1917; in 1918 was commissioned lieutenant colonel in the National army and reverted to his permanent rank of major in 1920; retired in 1922 and promoted to lieutenant colonel retired in 1930; aged 62; died, January 3, of ruptured duodenal ulcer and peritonitis.

Henry Maynadier Fitzhugh ● Westminster, Md.; University of Maryland School of Medicine, Baltimore, 1897; member of the House of Delegates of the American Medical Association, 1933-1934; president of the Federation of State Medical Boards of the United States; since 1910 member and since 1924 secretary and treasurer of the state board of medical examiners; in 1930 president of the Medical and Chirurgical Faculty of Maryland; president of the state board of education; aged 59; died, January 25, in the University Hospital, Baltimore, of acute streptococcic osteomyelitis of the femur.

Edmund Brown Piper ● Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1911; professor of obstetrics at his alma mater and the graduate school of medicine; member of the American Gynecological Society; fellow of the American College of Surgeons; served during the World War; obstetrician to the Pennsylvania Hospital and Hospital of the University of Pennsylvania; gynecologist to the Philadelphia General Hospital; consulting obstetrician to the Bryn Mawr (Pa.) Hospital; aged 53; died, January 14, of angina pectoris.

Thomas Morris Murray, Pomfret Center, Conn.; University of Maryland School of Medicine, Baltimore, 1873; at one time emeritus professor of physical diagnosis, laryngology and rhinology, Georgetown University School of Medicine, Washington, D. C.; formerly on the staffs of the Emergency and Garfield hospitals, Washington; aged 83; died, Dec. 16, 1934, of coronary thrombosis, diabetes mellitis and cirrhosis of the liver.

Alfred Goldstein Nadler, New Haven, Conn.; Yale University School of Medicine, New Haven, 1896; member of the Connecticut State Medical Society; clinical professor of dermatology at his alma mater; member of the New England Dermatological Society and the American Roentgen Ray Society; on the staffs of the New Haven Hospital and St. Raphael's Hospital; aged 61; died, January 14, of heart disease.

Albert James Welch ● Kansas City, Mo.; Starling Medical College, Columbus, 1894; past president of the Jackson County Medical Society; councilor to the thirteenth district of the Missouri State Medical Association; served during the World War in the public health department stationed at Washington, D. C.; aged 67; on the staff of St. Joseph's Hospital, where he died, Dec. 15, 1934, of coronary heart disease.

Oscar L. Norsworthy, San Antonio, Texas; Tulane University of Louisiana Medical Department, New Orleans, 1895; member of the State Medical Association of Texas; fellow of the American College of Surgeons; formerly member of the board of health of Houston; director of radium and cancer division, Medical and Surgical Hospital; aged 63; died, January 5, in Los Angeles, of heart disease.

Bertram H. Buxton, Byfleet, Surrey, England; New York University Medical College, 1897; in 1898 instructor in bacteriology, in 1903 associate professor of biology and in 1904 to 1912 professor of experimental pathology, Cornell University Medical College, New York; formerly on the staff of the Memorial Hospital for the Treatment of Cancer and Allied Diseases; aged 80; died, Dec. 6, 1934.

Richard Penn Smith ● Captain, U. S. Army, retired, Philadelphia; Temple University School of Medicine, Philadelphia, 1912; veteran of the Spanish-American and World wars; entered the medical corps of the U. S. Army in 1920 and retired in 1928 for disability in line of duty; aged 59; on the staffs of the Germantown Hospital and the Temple University Hospital, where he died, Dec. 23, 1934, of hypertension and nephritis.

William Fitzhugh Carter ● Major, U. S. Army, retired; Crozet, Va.; University of Virginia Department of Medicine, Charlottesville, 1872; entered the army as assistant surgeon in 1879 and was promoted through the various grades to that of major in 1897; retired in 1909 at his own request after thirty years' service; aged 84; died, January 1, in Richmond, of lobar pneumonia.

John Rowan Morrison ● Louisville, Ky.; Louisville Medical College, 1898; formerly adjunct professor of medicine and clinical medicine, University of Louisville School of Medicine; fellow of the American College of Physicians; on the staffs of the Norton Memorial Infirmary and St. Joseph's Infirmary; aged 57; died, January 8, of arteriosclerosis.

George Morley Marshall ● Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1886; formerly associate professor of laryngology, University of Pennsylvania Graduate School of Medicine; fellow of the American College of Surgeons; otolaryngologist to St. Joseph's Hospital; aged 76; died, January 8, of heart disease.

Howard Donald Urquhart ● New York; University and Bellevue Hospital Medical College, New York, 1906; formerly clinical professor of orthopedic surgery, New York Polyclinic Medical School and Hospital; formerly on the staff of the Seaside Hospital, Staten Island; aged 55; died, Nov. 8, 1934, of heart disease.

Jacob William Holderman, Duluth, Minn.; Rush Medical College, Chicago, 1918; member of the Minnesota State Medical Association; formerly resident in laryngology and otology at his alma mater; on the staffs of St. Mary's and St. Luke's hospitals; aged 44; died suddenly, January 22, of coronary thrombosis.

Warren Wallace St. John ● Troy, N. Y.; Columbia University College of Physicians and Surgeons, New York, 1905; past president of the Rensselaer County Medical Society; president of the hospital staff of the Samaritan Hospital; aged 52; died, Dec. 22, 1934, of cerebral thrombosis and cerebral arteriosclerosis.

Charles Egbert Willard, Catskill, N. Y.; College of Physicians and Surgeons, Medical Department of Columbia College, 1869; member of the Medical Society of the State of New York; for many years treasurer of Green County, and village health officer; aged 88; died, January 12, of arteriosclerosis.

John Harvey Graff, Perryville, Mo.; Chicago College of Medicine and Surgery, 1916; served during the World War; for many years connected with the U. S. Public Health Service; aged 41; died, January 6, in the Veterans' Administration Facility, Jefferson Barracks, following a thyroidectomy.

Beverley Z. Milner, Toronto, Ont., Canada; Trinity Medical College, Toronto, 1889; for many years on the staffs of the Toronto General Hospital and the Hospital for Sick Children; aged 69; was found dead, slumped over the steering wheel of his automobile, Dec. 7, 1934, of heart disease.

Oscar Simon Hornick, Brooklyn; University and Bellevue Hospital Medical College, New York, 1928; member of the Medical Society of the State of New York; aged 34; on the staff of the Israel Zion Hospital, where he died, January 7, of osteomyelitis of the jaw and cerebral abscess.

Edward Smith Winslow, Harwich Port, Mass.; Dartmouth Medical School, Hanover, N. H., 1892; member of the Massachusetts Medical Society; served during the World War; on the staff of the Cape Cod Hospital, Hyannis; aged 68; died, Dec. 28, 1934, of cerebral hemorrhage.

James M. Shields ● Seymour, Ind.; Kentucky School of Medicine, Louisville, 1881; president of the Jackson County Medical Society; formerly mayor of Seymour; formerly on the staff of the Schneck Memorial Hospital; aged 75; died suddenly, Nov. 30, 1934, in New York.

John Howard Wyman, Medway, Mass.; Harvard University Medical School, Boston, 1906; served during the World War; medical examiner of Norfolk County; aged 55; on the staff of the Milford (Mass.) Hospital, where he died, Dec. 17, 1934, of cerebral hemorrhage.

Homer Monroe Mace, Peekskill, N. Y.; University of the City of New York Medical Department, 1890; member of the Medical Society of the State of New York; aged 70; on the staff of the Peekskill Hospital, where he died, January 6, of splenic infarct and leukemia.

Wilton McCarthy, Des Moines, Iowa; Drake University Medical Department, Des Moines, 1894; member of the Western Surgical Association; fellow of the American College of Surgeons; formerly professor of clinical surgery at his alma mater; aged 62; died, Dec. 14, 1934.

Charles Lincoln Mohn, Jersey Shore, Pa.; College of Physicians and Surgeons, Baltimore, 1885; member of the Medical Society of the State of Pennsylvania; for many years on the staff of the Jersey Shore Hospital; aged 70; died, Dec. 19, 1934, of heart disease.

Benjamin Franklin McMillan, Red Springs, N. C.; University of Maryland School of Medicine, Baltimore, 1882; member of the Medical Society of the State of North Carolina; formerly member of the state legislature; aged 81; died, January 14, of pneumonia.

Peter Alfred Kearney, San Francisco; Cooper Medical College, San Francisco, 1884; at one time superintendent of the San Francisco County Hospital; aged 87; died, Dec. 15, 1934, in the Alameda (Calif.) Sanatorium on the South Shore, of coronary thrombosis.

Alvin Barney Eberhart, McDonough, Ga.; Emory University School of Medicine, Atlanta, 1922; member of the Medical Association of Georgia; served during the World War; aged 44; died, Dec. 28, 1934, of gastric hemorrhage resulting from carcinoma.

Frank Eli Hurrle, Little Rock, Ark.; University of Arkansas School of Medicine, Little Rock, 1911; also a pharmacist; member of the Arkansas Medical Society; aged 53; died, January 14, in a local hospital of injuries received in an automobile accident.

Henry Jeter Edmonds, Kilmarnock, Va.; University of Maryland School of Medicine, Baltimore, 1887; member of the Medical Society of Virginia; past president of the Northern Neck Medical Society; aged 68; died, Dec. 13, 1934, of cerebral hemorrhage.

Thomas Melchor Meisenheimer, Charlotte, N. C.; Medical College of the State of South Carolina, Charleston, 1925; member of the Medical Society of the State of North Carolina; aged 37; died, January 4, in the New Charlotte Sanatorium, of leukemia.

Leonidas A. Suggs, Park Place, Ore.; Vanderbilt University School of Medicine, Nashville, Tenn., 1892; member of the State Medical Association of Texas; past president of the Tarrant (Texas) County Medical Society; aged 70; died, Dec. 7, 1934.

Robert Andrew Poynton, Chicago; Niagara University Medical Department, Buffalo, 1891; on the associate staff of the South Chicago Hospital; aged 69; died, January 22, of uremia, cerebral arteriosclerosis and subacute coronary thrombosis.

W. Francis B. Wakefield, Los Gatos, Calif.; Trinity Medical College, Toronto, Ont., Canada, 1893; University of Toronto Faculty of Medicine, Toronto, 1893; fellow of the American College of Surgeons; aged 68; died, Dec. 4, 1934.

Joseph Albertus Hedding, Minneapolis; Minneapolis College of Physicians and Surgeons, 1906; member of the Minnesota State Medical Association; on the staff of St. Barnabas Hospital; aged 51; died, Dec. 26, 1934, of hypertension.

Jesse Gulledge, Tallassee, Ala.; University of Alabama Medical Department, Mobile, 1900; member of the Medical Association of the State of Alabama; aged 61; died, Dec. 19, 1934, in the Community Hospital, East Tallassee.

James I. Miller, Huntington, W. Va.; College of Physicians and Surgeons, Baltimore, 1906; aged 55; died, January 6, in a local hospital, of pneumonia, as the result of burns received in a gas explosion in the basement of his home.

John Auldo, Philadelphia; Jefferson Medical College of Philadelphia, 1882; formerly demonstrator of physical diagnosis and clinical medicine, Medico-Chirurgical College of Philadelphia; aged 88; died, Dec. 23, 1934.

Clarence C. Spicher ● Johnstown, Pa.; Baltimore Medical College, 1903; aged 62; chief on the medical service of the Conemaugh Valley Memorial Hospital, 1921-1934, where he died, January 1, of heart disease.

Lewis Joseph Hammers, Goodland, Kan.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; aged 57; died, January 19, of angina pectoris and coronary thrombosis.

Josiah Winslow Edgerly, New York; University and Bellevue Hospital Medical College, 1899; member of the Medical Society of the State of New York; aged 62; died, January 14, of lymphatic leukemia.

George Alexander Angus, Denver; Denver Homeopathic College, 1906; aged 64; died, Dec. 11, 1934, in the Denver General Hospital, of ataxic paraplegia, chronic pernicious anemia and myocarditis.

Rankin Robert Lowery, Augusta, Ga.; Atlanta Medical College, 1916; served during the World War; aged 43; died, Dec. 23, 1934, in Veterans' Administration Facility, of epidemic (lethargic) encephalitis.

Frederick Huhns, Kingston, N. Y.; University of Vermont College of Medicine, Burlington, 1884; for many years member of the board of health of Kingston; aged 78; died, January 4, of chronic arteriosclerosis.

Charles Webb Sheppard, Honoraville, Ala.; Southern Medical College, Atlanta, 1891; member of the Medical Association of the State of Alabama; aged 73; died, Dec. 9, 1934, of acute nephritis.

Daniel A. Wilson Sr., Norristown, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1890; served during the World War; aged 67; died, Dec. 22, 1934, of cerebral hemorrhage.

Reginald James Peer, Bangor, Maine; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1930; aged 29; died, Nov. 12, 1934, of morphine sulphate poisoning, self administered.

Ellery Newell Peck ● Boonton, N. J.; Cornell University Medical College, New York, 1904; served during the World War; aged 55; died, Dec. 20, 1934, in the Deaconess Hospital, Brookline, Mass.

James E. W. Price, Kingston, Tenn.; University of Tennessee Medical Department, Nashville, 1899; member of the county board of education; also a pharmacist; aged 68; died, Dec. 4, 1934.

Patrick H. O'Connor, Amboy, Minn.; Kansas City (Mo.) Hahnemann Medical College, 1906; member of the Minnesota State Medical Association; aged 56; died, Dec. 25, 1934, of heart disease.

Gustave Julius Dierkes ● Winona, Minn.; John A. Creighton Medical College, Omaha, 1917; on the staff of the Winona General Hospital; aged 43; died, Dec. 9, 1934, of pneumonia.

Irving S. Freeman, Rocky, Okla.; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1913; aged 49; died, Dec. 27, 1934, in Tulsa, of bronchopneumonia.

Henry Lee Yoder ● Morton, Ill.; Missouri Medical College, St. Louis, 1899; aged 62; died, Nov. 21, 1934, in the John C. Proctor Hospital, Peoria, of prostatic obstruction and pyonephrosis.

Joseph P. Morris, St. Clair, Pa.; Jefferson Medical College of Philadelphia, 1896; member of the Medical Society of the State of Pennsylvania; aged 61; died suddenly, Dec. 2, 1934.

Isaiah Thomas Harbour, Cowlington, Okla.; Kentucky School of Medicine, Louisville, 1888; aged 82; died, January 11, in Fort Smith, Ark., of adenocarcinoma of the pancreas.

Martha Louise Dedrick Bayles, Townsend, Mont.; University of Illinois College of Medicine, Chicago, 1930; aged 28; died January 6, in St. John's Hospital, Helena, of septicemia.

Hugh Sawyer James, McArthur, Ohio; Columbus Medical College, 1890; member of the Ohio State Medical Association; served during the World War; aged 69; died, Nov. 15, 1934.

Clara T. Dercum, Philadelphia; Woman's Medical College of Pennsylvania, Philadelphia, 1887; for many years on the staff of the Woman's Hospital; aged 76; died, Dec. 23, 1934.

John Thomas Deomar, Kittanning, Pa.; Jefferson Medical College of Philadelphia, 1879; member of the Medical Society of the State of Pennsylvania; aged 80; died, Dec. 9, 1934.

James Dennis, Albuquerque, N. M.; Howard University College of Medicine, Washington, 1906; aged 52; died, Dec. 23, 1934, of bronchopneumonia following a prostatectomy.

Frank Van Rensselaer Phelps, New York; Bellevue Hospital Medical College, New York, 1893; aged 68; was found dead in his automobile, January 9, of heart disease.

Irving Cyrus Blaisdell, Wilmore, Pa.; Bellevue Hospital Medical College, New York, 1871; aged 90; died, Dec. 12, 1934, of cardiac decompensation and bronchopneumonia.

Louis M. Hanemann, New Orleans; Tulane University of Louisiana Medical Department, New Orleans, 1891; aged 65; died, January 8, of cardiovascular renal disease.

William Frederick Marten, Ferguson, Mo.; Hahnemann Medical College and Hospital, Chicago, 1903; aged 46; died, Dec. 31, 1934, of a self-inflicted bullet wound.

John Anthony Regan, Scranton, Pa.; Chicago Medical School, 1934; aged 30; died suddenly, Dec. 27, 1934, in the Scranton State Hospital, of diabetes mellitus.

William A. Powel, Hernando, Miss.; College of Physicians and Surgeons, Baltimore, 1886; aged 72; died, January 5, of injuries received in an automobile accident.

John Kelly Moeur, Tempe, Ariz.; University of Illinois College of Medicine, Chicago, 1928; aged 37; died, Nov. 30, 1934, in St. Joseph's Hospital, Phoenix.

James A. Melvin, Baltimore; University of Maryland School of Medicine, Baltimore, 1887; aged 71; died, Dec. 6, 1934, in the Union Memorial Hospital.

Abel Mathias, Rapid City, S. D.; University of Pennsylvania School of Medicine, Philadelphia, 1865; aged 91; died, Nov. 11, 1934, of cerebral hemorrhage.

John P. Williams, Minneapolis; Chicago Medical College, 1876; aged 88; died, Nov. 11, 1934, of coronary sclerosis, arteriosclerosis and chronic nephritis.

Augustus P. Kempton ● Philadelphia; Jefferson Medical College of Philadelphia, 1880; aged 79; died, Dec. 6, 1934, in Ventnor, N. J., of chronic nephritis.

John Patrick Mulrenan ● Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1897; aged 64; died, January 5, of heart disease.

Samuel Lewis Wilkinson ● Belen, N. M.; University of Arkansas School of Medicine, Little Rock, 1907; aged 54; died, Dec. 30, 1934, of angina pectoris.

Ephraim Daniel McKenna, Oneonta, N. Y.; University of Vermont College of Medicine, Burlington, 1887; aged 75; died, January 13, of nephritis.

John C. Ware, Yellville, Ark.; Arkansas Industrial University Medical Department, Little Rock, 1886; aged 85; died, Nov. 5, 1934, of heart disease.

George Blatchford, Clinton, Mich.; University of Michigan Homeopathic Medical School, 1884; aged 87; died, January 2, of chronic myocarditis.

John Duncan, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1906; M.R.C.S., England, 1907; aged 59; died, Nov. 22, 1934.

William Scholes Kimmell, Uniontown, Pa.; Medico-Chirurgical College of Philadelphia, 1901; aged 65; died, Nov. 21, 1934, of paralysis agitans.

David Heist Wentz, Philadelphia; University of Pennsylvania School of Medicine, Philadelphia, 1883; aged 76; died, Dec. 27, 1934, of pneumonia.

A. Marshall Haas, Bunkie, La.; Tulane University of Louisiana Medical Department, New Orleans, 1896; coroner; aged 61; died, Dec. 13, 1934.

Frank Busby Parker, Ursa, Ill.; Keokuk (Iowa) Medical College, 1893; aged 63; died, Dec. 10, 1934, in St. Mary Hospital, Quincy, of encephalitis.

Simon J. Hampshire, Overbrook, Kan.; College of Physicians and Surgeons, Keokuk, Iowa, 1884; aged 74; died, Oct. 31, 1934, of arteriosclerosis.

Maurice R. Perlstein, Chicago; Chicago College of Medicine and Surgery, 1914; aged 43; died, January 21, of hydronephrosis and myocarditis.

David A. Maxwell, Lockesburg, Ark.; Memphis (Tenn.) Hospital Medical College, 1889; aged 78; died, Nov. 18, 1934, of cerebral hemorrhage.

Lewis Augustus Williams, Huntington, W. Va.; Medical College of Ohio, Cincinnati, 1891; aged 70; died, Dec. 27, 1934, of gastric carcinoma.

Michael Joseph Brown, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1920; aged 41; died, Nov. 11, 1934, of heart disease.

Henry John Plens, Chicago; Northwestern University Medical School, Chicago, 1910; aged 46; died, January 14, of organic heart disease.

Thomas P. W. Brooks, Hackleburg, Ala.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1897; aged 87; died, Dec. 15, 1934.

Manassa Thomas Pope, Raleigh, N. C.; Leonard Medical School, Raleigh, 1886; died, Nov. 13, 1934, of strangulated hernia and cystitis.

John Henry Watson, Toronto, Ont., Canada; Victoria University Medical Department, Coburg, 1869; aged 87; died, Nov. 16, 1934.

William Oscar Sauermann ● Houston, Texas; University of Michigan Medical School, Ann Arbor, 1893; aged 67; died, Nov. 26, 1934.

Simon Cameron Bowes, Canonsburg, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1893; aged 70; died, Dec. 17, 1934.

Everett A. Wood, Los Angeles; Keokuk Medical College, 1895; aged 70; died, Dec. 10, 1934, in the Los Angeles General Hospital.

Napoleon Wagner, Denver; St. Louis College of Physicians and Surgeons, 1884; also a lawyer; aged 76; died, Nov. 15, 1934.

Charles Mikula, Dwight, Kan. (licensed in Kansas in 1901); aged 72; died, Dec. 14, 1934, of carcinoma of the stomach.

Geoffrey Boyd, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1891; aged 65; died, Dec. 22, 1934.

James Archibald Hamilton, Winnipeg, Manit., Canada; Manitoba Medical College, Winnipeg, 1904; died, Dec. 26, 1934.

Dennis P. Russell, Chicago; Rush Medical College, Chicago, 1890; aged 74; died, January 15, of cirrhosis of the liver.

Thomas Nathan Eblen, Orme, Tenn.; Chattanooga (Tenn.) Medical College, 1899; aged 62; died, January 5, of pneumonia.

Robert S. Medearis, North Little Rock, Ark. (licensed in Arkansas in 1903); aged 64; died, Dec. 8, 1934.

John G. Chessher, Falco, Ala.; Chattanooga (Tenn.) Medical College, 1901; aged 76; died, Nov. 17, 1934.

Bureau of Investigation

AMERICAN INSTITUTE OF MEDICINE AND SURGERY, INC.

An Impudent Scheme Designed to Capitalize the Vanity of Physicians and Others

In December, 1934, news items began appearing in newspapers—usually those published in the smaller towns—regarding an alleged "honor" that had been conferred upon some local citizen by the "American Institute of Medicine and Surgery" at a meeting of the "nominating committee" in New York. Such local celebrities appeared at first to be mainly optometrists, although the list has since been extended to cover osteopaths and physicians.

Following the appearance of the local news item, the person whose name was mentioned would receive a letter informing him in detail of the alleged honor and asking him to sign a "pledge" that is enclosed, and to return it with a check or money order for $25, on receipt of which the American Institute of Medicine and Surgery would send a handsome certificate for framing and hanging in the reception room!

Some of the members of the American Optometric Association, recognizing that as they practice neither medicine nor surgery the alleged honor that was said to have been conferred on them was obviously undeserved, questioned the bona-fides of the imposingly named "Institute." As a result, the *Optometric Weekly* published in its issue of Dec. 27, 1934, a warning item entitled "Look Out for This Racket."

This probably interfered with the success of the scheme among optometrists and may explain why osteopaths and physicians were then worked on.

The news items already referred to have appeared in various parts of the United States, ranging from Florida to California. The letter that the individuals whose names were published in the local papers received from the so-called American Institute of Medicine and Surgery, Inc., of 150 Nassau St., New York City, read as follows:

> *"Dear Doctor:*—It is my privilege to announce that the Board of Directors has qualified you for a life-time honorary membership in the American Institute of Medicine and Surgery. This is to take effect upon your signing the inclosed pledge and fulfilling the usual preliminary requirements of honorary membership.
>
> "Because the American Institute of Medicine and Surgery is a non-profit making corporation, there are no annual dues. One initiation fee of Twenty-five dollars ($25.00) alone is required from each honorary member.
>
> "Please sign your name to the inclosed pledge and print your name plainly below in the form you wish it to appear on the Certificate of Honorary Membership, a facsimile of which is printed on the pledge. The Certificate, as it is sent to you, is 14 inches by 17 inches in size, and may be framed and hung in the reception room of your office, thereby showing, to whom it may concern, that you have been signally honored by this organization.
>
> "We heartily congratulate you upon your selection as an outstanding representative of your profession in your district, and trust that you will, at your earliest convenience, return the pledge, properly signed, together with check or money order to cover the initiation fee."

Accompanying the letter, which was signed "John J. Caldwell, Secretary," was a miniature reproduction of the "certificate of honorary membership" for which the optometrist, osteopath or physician was asked to send $25; there was also the "honorary membership pledge," which the recipient was asked to sign and return with his $25.00. The "pledge" read as follows:

> "I pledge myself to maintain the highest ethics of my profession and to do all within my power to bring a new era of physical and mental well-being to the peoples of the world.
>
> "With True Appreciation of the dignity, nobility and sacrifice of this, my life work, I sign my name to this pledge."

There was the inevitable dotted line just below the "pledge" for the signature of the person to whom it was sent. The "certificate" itself is reproduced with this article, in order to give a general idea of the character of the piece of paper for which physicians and others are expected to pay $25. Because of the great reduction in size made necessary by the limitations of space, the wording of this certificate is here reproduced:

> "Proceedings in Council: By Virtue of Eminent and Laudable Service in the Cause of Healing, the Alleviation of Human Suffering and Advancement of the Dignity and Honor of the Profession, and in Recognition of Fidelity to the Highest Ideals and Ethical Standards in the Research for Knowledge and the Discharge of Professional Duties, and for Lasting Devotion to the Most Just Principles in Striving for the Physical and Spiritual Betterment of the Race,
>
> Be it known that
> JOHN HENRY SMITH
>
> Has Been and Is Nominated and Approved as Honorary Member of the Institute, Whereof this Certificate is Testimonial. This 10th Day of the Month of November in the Year of Our Lord 1934. Done under the Seal of the American Institute of Medicine and Surgery, Incorporated (not for profit) in Accordance with the Usages and Laws of the State of Delaware."

The certificate is signed by the "President," "Secretary" and "Chairman, Committee on Honors." As well as can be deciphered from the reproduction sent out, the president's name appears to be Robert V. Steele; the secretary's John J. Caldwell

Reproduction (greatly reduced—the originals are 14 inches by 17 inches) of the "Certificate of Honorary Membership" which the "American Institute of Medicine and Surgery, Inc." attempts to sell to optometrists, osteopaths and physicians for $25.00. The alleged "institute" does not exist except on paper. What the certificate actually certifies to is that the possessor is an easy mark or a poseur.

—whose name also appears in connection with the letter—and that of the chairman of the "Committee on honors" [1] E. L. Fogelsonger.

The American Institute of Medicine and Surgery, Inc., was not to be found in any record possessed by the Bureau of Investigation; it was obviously a new humbug. Neither did one find the names of Steele, Caldwell or Fogelsonger.

From investigation it appears that the so-called American Institute of Medicine and Surgery, Inc., is a New York organization incorporated in November, 1934, with no stated authorized capital; that Fogelsonger is the dominating factor in the enterprise and that he is alleged to have formerly been financially interested in the "Book Craft Guild"—whatever that may have been—said to have been established in April, 1932, but now to be out of business. The headquarters of this imposingly-named outfit were simply rented quarters in Room 736 in the office building at 150 Nassau Street. Efforts to obtain an interview with Fogelsonger were fruitless, and no one could be found who either had, or was willing to furnish, information on which an estimate of the responsibility of the concern could be determined. Further help was sought through both the National Better Business Bureau and the Better Business

Bureau of New York City. The latter organization reported that the post-office officials were investigating and that both Caldwell and Fogelsonger had disappeared. It reported, also, that Ann Lord, a reputed publicity agent at 53 Park Row, had a mailing address there, but her identity was unknown.

A search of the files of the Bureau of Investigation failed to show any record of any "Ann Lord" as a publicity agent. There was a record of one Annie Lord, who has sometimes, it appears, gone by the title "Dr." In 1933 there was one Annie Lord who called herself a "Consulting Psychologist," operating from Studio 603, Carnegie Hall, New York City. Then there was an Annie Lord whose advertisement was published in the Chicago *Tribune* April 17, 1932, in which the lady was described as an "Eminent Business Analyst of Washington, D. C." The Bureau also has a record of one Annie Lord, a "naturopath," who in 1928 was prosecuted and found guilty of practicing medicine without a license by the state authorities of New Jersey. A news item to this effect was published in THE JOURNAL July 28, 1928. None of these Annie Lords, however, seem to fit in with the Ann Lord referred to by the Better Business Bureau of New York City. In fact, a later letter from that organization reported that the current telephone directory of New York City carried the name "Annie Lord, Psychic" at 210 West 72d Street.

As the "certificate" of the American Institute of Medicine and Surgery definitely states that the concern is a Delaware corporation, the Bureau of Investigation asked the Secretary of State of Delaware, for the names of the officers and incorporators. The secretary replied on January 16, 1935 that (1) the "institute" was incorporated August 6, 1934, but the annual report showing the names of the officers had not yet been filed; (2) the Capital Trust Co. of Delaware was the resident agent and (3) the incorporators were: Robert V. Steele, 2449 28th St., Astoria, L. I., N. Y. John J. Caldwell, 68 East 90th St., New York City. Fogelsonger (no given name or initials), 165 W. 87th St., N. Y. C.

The Better Business Bureau of New York City reported, further, that on January 21 Post Office Inspector Frank Shea had instructed Fogelsonger to call at his office, at which time a representative of the Better Business Bureau of New York City was present. The entire matter was submitted to Mr. Pfann, Assistant United States Attorney, who, after reviewing the facts, is reported to have told Fogelsonger that while there was not at present sufficient evidence to warrant prosecution for a mail-order fraud, Fogelsonger, Caldwell and Steele were heading for trouble. None of the three men back of the scheme are physicians or have any interest in the medical profession—other, presumably, than the effort to get $25 from certain members of that profession.

The scheme is not original. Nearly forty years ago a quack named Probert sold from Niles, Michigan, so-called "Certificates of Merit" from the fake "St. Luke's Hospital" of that city. After the Michigan legislature outlawed this swindle the name and locality was changed and it became the "Christian Hospital" of Chicago. A quarter of a century ago many of these "certificates" adorned the walls of advertising quacks. Then there was the imposingly named "Incorporated Society of Science, Letters and Art of London," an English swindle that sold "Fellowships" to all and sundry at one guinea ($5.00) apiece. These permitted the owners to write the mystic letters "F.S.Sc.(Lond.)" after their names, which many American "patent medicine" exploiters did. In Italy there was the "Italian Physio-Chemical Society" of Palermo which sold "diplomas" at $5.00 and "First Class Medals for Technical Work and Scientific Merit" for $10.00 to vainglorious or gullible Americans.

One needs waste no sympathy on physicians, osteopaths or optometrists who have parted with $25.00 for the gaudy piece of paper sold by Messrs. Steele, Caldwell and Fogelsonger and obviously designed to deceive the public and appeal to the vanity of the purchasers. It is obvious that "membership" in American Institute of Medicine and Surgery, Inc., simply means that the "member" is either an easy mark or a poseur who would assume an erudition he does not possess, or both.

Queries and Minor Notes

ANONYMOUS COMMUNICATIONS and queries on postal cards will not be noticed. Every letter must contain the writer's name and address, but these will be omitted, on request.

DETERMINATION OF HEMOGLOBIN

To the Editor:—There has been a considerable amount of controversy regarding the determination of hemoglobin. At the present time I am using the improved Sahli instrument, graduated in per cent and in grams per hundred cubic centimeters, 14.5 Gm. per hundred cubic centimeters being the equivalent of 100 per cent. It has also been my practice to estimate the color index by using percentage rather than Sahli units. The latter were used on the tubes formerly supplied and having a circular cross section. It is claimed that my hemoglobin determinations are too high and that Sahli units should be used for this purpose. Just what does a Sahli unit indicate? I am anxious to know this, particularly because I am contemplating the purchase of a new instrument. Please omit name.

M.D., New York.

ANSWER.—Much of the controversy that exists regarding the determination of hemoglobin is due to the method employed or the manner in which the results are expressed. There are now on the market several accurate hemoglobinometers that may be conveniently used for office practice. Unless these have been carefully checked before leaving the factory, however, inaccuracies may arise. Errors in the bore and graduation of the tube and pipet may contribute to wrong values. Despite the precaution in providing an accurate instrument, discrepancies may arise also in the manner of expressing hemoglobin values. Formerly hemoglobin was expressed by an empirical scale of per cent and Sahli units. For example, the old Sahli tube had a scale showing Sahli units and opposite this was a per cent scale for those who prefer to express their results by this designation. The 100 per cent mark was opposite 80 Sahli units. These two readings had a value of 17 Gm. of hemoglobin per hundred cubic centimeters of blood. Different hemoglobinometers also graduated in per cent gave different values on the same sample of blood. The confusion lay not in the method of determination but in the lack in agreement as to how many grams of hemoglobin constituted 100 per cent. As an illustration of this situation the following values have been suggested as being equal to 100 per cent: Dare (new), 16.0 Gm.; Haldane, 13.8 Gm.; Tallqvist, 15.8 Gm.; Haden, 15.6 Gm.; Osgood, 14.6 Gm., and Wintrobe, 14.5 Gm. Obviously, unless one knew the method by which per cent was determined and reduced to a common factor such as grams per hundred cubic centimeters of blood, there would be considerable disagreement even on the same sample of blood. Because of the potential confusion when values are reported in per cent without stating the standard on which it is based, it has been urged that hemoglobin be reported in grams per hundred cubic centimeters of blood. Theoretically, this would avoid confusion regardless of what instrument is used. Practically, however, there are still discrepancies, because the various methods are not all carefully standardized and accurate, and errors in technic also may arise. Therefore, it is best when purchasing a hemoglobinometer to find out whether it has been carefully checked against the Van Slyke oxygen capacity method or the more accurate methods for iron determination and standardized. It should also be as free as possible from any potential technical error. The instrument that the correspondent has is satisfactory. The new Hellige Sahli is based on the recent work of Dr. M. M. Wintrobe and has been carefully checked and standardized. Because of the preference of some clinicians still to express hemoglobin in per cent, the tube is graduated in per cent as well as in grams. When the hemoglobin is expressed in per cent, 14.5 Gm. is used as the equivalent of 100 per cent. While the adoption of this value for 100 per cent gives a reliable color index, it yields high percentages for most adult males. The reason for this is that the hemoglobin values for normal male adults average about 16 Gm. per hundred cubic centimeters of blood, with from 14 to 18 Gm. as the limits of normal; adult women average 14 Gm., with a normal range of from 12 to 16 Gm. It is therefore preferable to express hemoglobin values in grams rather than in per cent. It may be that the correspondent's values are too high because he reports them in per cent based on 14.5 Gm. of hemoglobin per hundred cubic centimeters of blood as being equivalent to 100 per cent. If this is not the case it is advisable to make sure that the hemoglobinometer has been properly standardized.

ECZEMA OF AUDITORY CANAL

To the Editor:—A woman, aged 30, has chronic eczema of the external auditory canal of both ears. There is a constant desquamation, with considerable amounts of creamy moisture that has an unpleasant odor. There is intense itching and it is almost impossible for the patient to refrain from rubbing the mucous membrane, either with a twisted handkerchief or with a toothpick applicator. On thorough cleansing there is no abnormality except a slight thickening and marked redness of the lining of the canal. There are no foci of infection; the patient is perfectly healthy in every respect, except that she may be hypersensitive to the slight odor of this aural discharge. The discharge is not excessive, but if it is allowed to remain for a few days the canal becomes partially filled with moist creamy looking scales, which produce a fetid odor. Under daily cleansing treatment the canal remains clean, but after two days or more the condition constantly recurs. I have tried every form of treatment that I have access to, such as boric acid powder insufflation, metaphen applied topically and by the pack method, quartz light treatment, salicylic acid in collodion painted on the mucosa, phenol and glycerin, and hydrogen dioxide and all that has been accomplished is a temporary relief from symptoms. Even when the patient leaves the canal strictly alone, a discharge and moist appearance of the mucosa will occur. I should like to know what more I can do for this woman. Please omit name.

M.D., Illinois.

ANSWER.—The quickest and cleanest method of giving relief would be roentgen rays, one-fourth erythema dose once a week. If this is not available, solution of aluminum acetate, 1 part to 16 parts of water, may be applied on a roll of cotton or gauze. When this has succeeded in stopping the discharge, 1 per cent salicylic acid and resorcinol in 30 per cent alcohol should be swabbed on frequently and allowed to dry on. The patient must refrain from scratching or rubbing, or the condition will not clear up. She should apply the lotion when tempted to scratch.

After the surface has ceased to weep, gentle applications with a swab, once or twice a day, should be made of rectified oil of birch tar, 0.8 cc., resorcinol, 0.4 cc., and liquid petrolatum, sufficient to make 16 cc. If this causes oozing or increased itching, it cannot be used. For soothing, 10 per cent boric acid in petrolatum should be used. If oozing recurs, the solution of aluminum acetate treatment should be resumed. If improvement ceases after a considerable use of the oil, the strength may be doubled, or ointment of rose water containing 5 per cent of coal tar solution and 2 per cent of salicylic acid may be substituted. For cleansing, oil or liquid petrolatum may be used. It must be expected that the dermatitis will return after a time. A definite cure of such a condition is hard to promise.

SINUS INTO ANTRUM

To the Editor:—About a year ago a man, aged 55, had a tooth extracted, and an infection of the antrum developed. There were the usual symptoms of pain and purulent discharge, for which he did nothing until several weeks elapsed and then I saw him, though only for a few times, as he thought that he could care for himself. Now he comes with a sinus that is quite open, with a little discharge, and expects it to be healed in a short time. Will you please give me the best treatment for it? Will irrigations do any good and also is curettement of the antrum indicated? Kindly omit name.

M.D., Minnesota.

ANSWER.—The fistula that occasionally develops after extraction of a tooth the root of which extends to or into the maxillary sinus is often resistant to treatments so far as closure is concerned. If there is a change in the mucosa of the antrum it would be necessary to operate either intranasally or by way of the canine fossa, removing all diseased tissue, freshening the edges of the fistula, and suturing. In some cases in which the changes in the antrum are not definite, a few irrigations followed by freshening of the edges of the mucosa of the fistula, and suturing, may suffice. In other cases it is impossible to approximate the edges of the mucous membrane without making a flap in order to effect the perfect closure of the opening leading into the antrum.

INTELLIGENCE OF CHILDREN WITH CONGENITAL SYPHILIS

To the Editor:—In THE JOURNAL, Nov. 24, 1934, appears the statement "for they are frequently somewhat above the ordinary in intelligence." in a query and minor note entitled "Child with Congenital Syphilis." It will be appreciated if you will kindly extend the statement in detail.

EDGAR C. HAYHOW, Paterson, N. J.
Superintendent, Paterson General Hospital.

ANSWER.—A statement regarding precocity in children with congenital syphilis deserves emphasis because of the tendency among the uninitiated to regard congenital syphilis as a principal cause of imbecility, feeblemindedness, idiocy, backwardness and mental retardation. White and Vieder in 443 cases found 15.7 per cent of mental retardation, including all grades from idiocy upward. The milder grades seem much the more common. In Stokes's series, 25 per cent were below par mentally, as expressed by slow progress in school and difficulties in adaptation. Twenty-two per cent of his patients exhibited heightened nervous irritability with emotional instability, fits of temper, night terrors, the easy development of tics and habit spasms, and the like. Twelve per cent of Stokes's series exhibited a mental development well beyond their years. In many cases, in spite of the handicaps of eye trouble and susceptibility to other illness, it was quite sufficient to place them well beyond the average in school. The Solomons call attention to the precocity observed in certain syphilitic children, with citation of a case illustration, but properly emphasize that this precocity does not indicate that syphilitic heredity is an asset but that the disease had no effect on this child's mentality. The general studies of Haines and of Bazeley and Anderson do not greatly clarify the problems of conduct disorder with which they deal in relation to syphilis but support the general view that the disease may markedly influence abnormalities in this field.

It is apparent, therefore, that the mental and nervous state of children with congenital syphilis may vary between idiocy and precocity, and that a sharp distinction must be drawn between the coincidence and the possible etiologic association between the syphilis and the mental state. At least it can be definitely shown, and is familiar to all syphilologists of experience, that a high degree of precocity is in no way inconsistent with the presence of a congenital syphilitic infection.

POSITION OF HEAD IN TONSILLECTOMY

To the Editor:—I should like to know whether it is feasible to have a patient during a tonsillectomy tilted head down at an angle of about 10 degrees. The most frequent serious complication of tonsillectomy is lung abscess due to aspiration during or shortly after the operation. The article by Smith (THE JOURNAL, September 29, p. 971), in which he stated that in thirty-nine cases of lung abscess thirteen followed tonsillectomy, prompted my query. Murphy (*Am. J. Obst. & Gynec.* 27:118 [Jan.] 1934) has shown that, in curarized cats kept alive in a respirator and tilted head down at an angle of from 15 to 20 degrees, fluid dropped into the trachea was not aspirated into the lungs. Probably the tendency to aspiration is greater in a respirator than during anesthesia when breathing is shallow. For that reason a patient might be tilted only 10 degrees or so to avoid aspiration. It may be that some surgeons do tilt their patients during tonsillectomy but I have seen only one do so and that was Dr. Sullivan of Mount Vernon. There may be some objection to such a procedure which I do not realize but it seems a simple prophylactic measure. After the operation the patient's bed could be tilted head down until he regains his cough reflex.

M. BERNARD BRANDY, M.D., Mount Vernon, N. Y.

ANSWER.—It would seem that there is no contraindication whatever to having the head tilted down when tonsillectomy is performed under general anesthesia. Many years ago the late Dr. F. Gurney Stubbs did all his operations in this manner without any difficulty so far as any postoperative complications were concerned. With the head tilted down, he and many other good operators were in the habit of sitting directly behind the patient instead of to one side, as is ordinarily done while the head lies flat on the table.

MANAGEMENT OF THYROID CRISES

To the Editor:—I am particularly interested in the use of compound solution of iodine (Lugol's solution) by the "intravenous route" both in thyroid crisis and as a routine procedure following thyroidectomy for hyperthyroidism. Has this method of administration been used to any extent and if so is there any literature to which I can refer? Please omit name.

M.D., New Jersey.

ANSWER.—The questions suggest that the inquirer believes that compound solution of iodine is a unique and necessary formula for the administration of iodine to patients with hyperthyroidism. Many studies now prove that iodine, in whatever form, is the effective agent. It is not necessary, therefore, to give compound solution of iodine intravenously; as a matter of fact, its chemical nature prohibits such usage. Potassium iodide in concentrated sterile solution—from pharmaceutical ampules or diluted in other fluids—given by venoclysis, may be given intravenously during thyroid crises. However, the instantaneous absorption of iodine from the gastro-intestinal tract makes the parenteral route unnecessary. A diluted compound solution of iodine may be given into the corner of the mouth with a medicine dropper; 13.6 cc. (200 minims a day of compound solution of iodine may thus be given. Examples of the management of thyroid crises are given by Paul Starr (The Course of Hyperthyroidism under Iodine Medication, *Arch. Int. Med.* 39:520 [April] 1927).

HEART DISEASE

To the Editor:—Mrs. A., aged 27, married nine years, has no children. The childhood history is negative except for tonsillar infections. The latter were treated subsequently by the electrocautery at the time of the cardiac infection. Several weeks after her marriage, about nine years ago, after having a subacute throat infection, she was suddenly taken ill with cardiac collapse, characterized by arrhythmia and extrasystoles. She was not then under my care, but the history of that illness was one of long duration (about nine months), little or no fever at onset, with negative blood cultures and throat cultures. The last three months included invalidism, continued asthenia and extrasystoles. The bearing of children was not advised. Since that original illness she has always experienced missing heartbeats with greater or less frequency, never being entirely free from them for more than some hours. Since then she has had several periods a year of acute relapse, being bedridden for weeks at a time, suffering from missing heartbeats and shortness of breath, the extrasystoles then always being accompanied by severe shock and a dry, hacking cough. I first treated the patient last spring, when she went through a relapse lasting about six weeks. When she is feeling comparatively well and strong the extrasystoles, though they occur, are not accompanied by cough, dyspnea or shock. But when she has a relapse, the missing heartbeats are extremely exhausting and the patient coughs continuously. She may have a period of feeling very well, and without any exciting cause her heart becomes bad and she commences to cough. The patient is well nourished and otherwise normal. The tonsils are now small and she rarely suffers from sore throats. The electrocardiogram, taken several times, is entirely normal as the extrasystoles disappear apparently when the pulse reaches 100, as a result of nervous excitement. Ordinarily her pulse is between 70 and 80. Sedatives have an uncertain action, as well as digitalis. Roentgen examination shows only a slightly enlarged heart. The lungs are normal. There are no cardiac murmurs. Even under morphine I have seen her cough and the heart miss for six to twelve hours. I would appreciate therapeutic suggestions and discussion of this case. Kindly omit my name in publishing.

M.D., New York.

ANSWER.—Heart disease at the age of 27, with the history of cardiac infection at the time of or following tonsillitis, suggests that this case is an example of chronic rheumatic carditis. This condition complicated by subacute bacterial endocarditis may well be the explanation of the continued invalidism and periodic acute exacerbations, even though blood cultures have been negative. Low fever, or its absence would not exclude this possibility, nor would the failure to observe embolic phenomena or splenic enlargement entirely remove the possibility from consideration.

However, from the description of the relapses, with dyspnea and cough, it would be easy to believe that recurrent congestive heart failure with passive congestion of the lungs is the cause. This, of course, is frequent in mitral stenosis. A disorder of cardiac mechanism, such as paroxysmal auricular fibrillation, might be responsible.

It is unlikely that extrasystoles in a normal mechanism would cause such a picture, even though they occur with great frequency. The fact that the patient complains of the heart missing suggests heart consciousness. Neurotic individuals frequently complain of extrasystoles even when there is no other impairment of cardiac function. On the other hand, many people who have frequent premature contractions either are unconscious of them or at least offer no complaint.

Digitalis is not indicated unless decompensation is present or imminent, because its effect on heart muscle irritability will increase the frequency of extrasystoles. Sedatives have relatively little effect on premature contractions. Quinidine might be useful, but only too often, even in large doses, it will not alter this type of arrhythmia. It is noted that increase in heart rate causes the rhythm to become regular. If there is no contraindication to its use, and extrasystoles are the main cause of complaint, desiccated thyroid in cautious doses may be helpful by increasing the heart rate to the point at which the arrhythmia disappears.

BED SORES

To the Editor:—A white patient, aged 28, had a fracture of the spine at the junction of the twelfth dorsal and first lumbar vertebrae, with a resulting paralysis. A body cast was applied for two months, and as a result large bed sores formed over the great trochanters of each femur, and over the area of the sacrum. These sores are cleansed each day with alcohol, and zinc oxide ointment is applied. The patient is given a balanced diet and insulin daily. Healing has been very slow. What suggestions have you for the treatment of these bed sores? This patient is at home, and hospitalization is out of the question because of the family's economic condition.

ADRIAN B. CAIRNS, M.D., Pollock, La.

ANSWER.—It is advisable to discontinue the daily cleansing with alcohol, as this might kill the new growth of cells. The ulcers probably require "stimulation," for which purpose balsam of peru is the time honored remedy. It may be applied full strength or mixed with castor oil in whatever proportion is required to subdue the burning sensation produced in the more sensitive ulcers. Especially stimulant to the growth of epithelium is scarlet red ointment (5 per cent), which might be applied on days alternating with the balsam of peru dressing. Thiocresol compresses have of late been advocated to stimulate healing of very extensive ulcers. A freshly prepared 1:10,000 solution (of the 2 per cent alcoholic stock solution, 5 cc. is mixed with 100 cc. of distilled water) is applied on gauze, which is then covered with waterproof material. This dressing is changed every two hours. To avoid excessive irritation, it is best alternated with compresses of physiologic solution of sodium chloride at possibly forty-eight hour periods. Skin grafting should be undertaken for all large ulcers as soon as a bed of healthy granulations has been secured; and the modern method of "seed implants" is so simple and uniformly successful that there should be no hesitancy in resorting to it promptly.

USE OF WHOOPING COUGH VACCINE

To the Editor:—I have attempted recently to immunize a number of children against whooping cough. I have used a vaccine manufactured by Squibb & Sons, which is claimed to contain 10,000 million bacilli (Haemophilus pertussis) per cubic centimeter. The literature accompanying the vaccine recommends a dose of 0.5, 1 and 1.5 cc. at intervals of about five days, irrespective of age. I have given the children 0.5, 0.75 and 1 cc. subcutaneously at five day intervals and have had a number of rather severe general and local reactions. The reactions consist of fever, nausea, vomiting, diarrhea, malaise and occasionally a cough. The local reactions consist of redness, swelling and pain. I would appreciate an opinion of the following questions: Does the present status of pertussis vaccine warrant its use as an immunizing agent? Would the use of the higher dosage, as recommended, be likely to give rise to reactions of a serious nature? Please discuss accepted dosage. Kindly omit name.

M.D., New York.

ANSWER.—The Council on Pharmacy and Chemistry omitted in 1931 all pertussis vaccines from New and Nonofficial Remedies because "in twenty years no conclusive evidence had been accumulated regarding the therapeutic or prophylactic efficacy of such preparations." Recently Sauer (Whooping Cough: A Study in Immunization, THE JOURNAL, Jan. 28, 1933, p. 239; Immunization with Bacillus Pertussis Vaccine, Nov. 4, 1933, p. 1449) has brought the first convincing evidence that his vaccine, prepared from recently isolated, hemolytic strains, of the pertussis bacillus, grown on medium prepared with human blood, will confer prolonged immunity in a high percentage of young children, if injected at least several months before exposure. This vaccine is now available (Lilly's V. 374; Parke, Davis's Bio. 204). A total of 8 cc. (1, 1.5 and 1.5 cc. bilaterally) is given hypodermically, in the course of three successive weeks. Prepared without alien blood, local and systemic reactions, when they occur, are seldom severe and have never been serious in the seven years that it has been in use.

NEPHROPTOSIS AND URETERAL STRICTURE

To the Editor:—A white American woman, aged 31, a teacher, was laid up in the hospital for six weeks in May and June with an attack of acute bilateral pyelitis of Bacillus coli type. Last week a pyelogram was taken and it showed a general visceral ptosis, especially involving the left kidney. The left ureter was kinked and bound down, and near the pelvis of the kidney it was narrowed. It is being dilated now, and a kidney belt has been ordered from the United States. The urologist intends to dilate the ureter about four or five times. What I want to know is this: Are there any exercises that will tend to hold the kidneys in place? Are there any postural treatments that will supplement the action of the kidney belt and in time enable the patient to do without a belt, which is rather hard to wear in a tropical climate? The patient is 5 feet 6 inches (168 cm.) tall and weighs 130 pounds (59 Kg.). She has always been an active girl, swimming, riding horseback and bowling. Her musculature is good. Please omit name.

M.D., Canal Zone.

ANSWER.—There is no postural treatment that is of definite value in nephroptosis. It must be kept in mind, however, that patients must be instructed to apply the kidney belt while they are recumbent and not while they are standing. As a general rule, patients with nephroptosis are underweight. The administration of a high calory diet is indicated to increase the patient's weight, particularly to add to the renal fat. This may assist materially in the elimination of symptoms. The more strenuous exercises, such as riding horseback and bowling, should be avoided, but swimming may be permitted.

It is unusual for a patient to have both nephroptosis and ureteral stricture. In most instances the narrowing and kinking of the ureter is only an apparent one, which is the result of faulty technic in making the pyelogram. Unless there is evidence of back pressure such as dilatation of the renal pelvis and calices, it would be well to review the diagnosis.

The use of the ketogenic diet to eliminate the infection with colon bacilli may be all that is needed, and continued use of the belt might become unnecessary.

ADENOMA IN THYROID AND EFFECTS ON HEART MUSCULATURE

To the Editor:—Question has arisen locally as to whether the presence of an adenoma of the thyroid gland, whether associated with increased metabolic rate or not, existent over a period of years, should be a source of danger to the heart musculature. The question has arisen regarding a case in which a man is known to have had an adenoma of the thyroid gland over a period of twenty years and who in the last two or three years has developed cardiac decompensation. Lacking a specific cause, I wonder whether this adenoma, although causing no increase in metabolism, may not have been the underlying factor. I would appreciate your letting me have whatever references may appear in the literature on this subject.

J. Stuart Staley, M.D., Marion, Va.

Answer.—An adenoma of the thyroid gland associated with an increased metabolic rate is regarded by all observers as a cause of cardiac embarrassment. It is doubtful whether any form of thyroid disease of itself produces significant permanent organic changes in the heart muscle, or congestive heart failure. When the latter developments are found, there is almost always an additional and independent form of heart disease, such as a valvular, hypertensive, coronary artery or syphilitic process. Symptoms such as fibrillation, palpitation, dyspnea and weakness, however, can occur as a result of the thyroid disease alone. It is unlikely that an adenoma unassociated with toxicity or an increase in the metabolic rate is a significant danger to the heart musculature. But finding the basal metabolism within normal limits is no proof that it always has been normal, and plus 8.0 per cent may be 20 per cent above that patient's normal rate if he started from a minus 12 per cent. Furthermore, there are certain "toxic" effects that are supposed to be due to the thyroid gland that are independent of the metabolic rate and may be going on when the metabolic determinations are normal. Following are references:

Coller, F. A.: The Morbidity of Endocrine Goiter, The Journal, May 31, 1924, p. 1745.
Barker, P. S.; Bohning, Anne L., and Wilson, F. N.: Auricular Fibrillation in Graves' Disease, *Am. Heart J.* **8**: 121 (Oct.) 1932.
Morris, R. S.: The "Thyroid Heart" with Low Basal Metabolic Rate, *Am. J. M. Sc.* **181**: 297 (March) 1931.
Levine, S. A., and Walker, G. L.: Further Observations on Latent Hyperthyroidism Masked as Heart Disease; Angina Pectoris, *New England J. Med.* **201**: 1021 (Nov. 21) 1929.

USE OF PITUITARY PREPARATIONS FOR INCREASING GROWTH

To the Editor:—Recently a well nourished girl of 12 asked me what I could do to increase her stature, which is decidedly short for her age. She is quite bright and does not complain of cold weather, so I did not have her basal metabolism taken. I know that pituitary preparations are sometimes used for this purpose but should like further information as to the method of administration by mouth or otherwise, dose, method of control, and efficiency and general advisability. Kindly omit name.

M.D., Colorado.

Answer.—It is not possible to determine the precise nature of the growth disturbance in this case. If it is assumed, however, that the patient is suffering from hypopituitarism (and it is known from animal experiments that the anterior lobe of the pituitary gland exercises control of bodily growth, particularly on bone development) the treatment of this child may be considered through the use of pituitary substances. The use of the dried anterior pituitary gland given by mouth, even in large doses, has usually failed to produce any results. Evans in 1921 showed that the simple watery extracts of the anterior pituitary glands of oxen injected into rats caused acceleration of growth. Later on, one of Evans's students working in Cushing's Laboratory at Harvard produced experimental acromegaly as well as an increase in size of the internal organs by injecting into dogs products containing the anterior pituitary growth hormone. A similar preparation may be given hypodermically in doses of 1 cc. daily. The preparation made by E. R. Squibb and Son containing the anterior pituitary growth hormone has been administered in doses of from 7 to 15 minims (0.4 to 0.9 cc.) intramuscularly once daily. Engelbach and Schaefer (The Journal, Aug. 18, 1934, p. 464) have treated seven cases of endocrine dwarfism by using the solution of the pituitary growth factor marketed by Parke, Davis & Co. under the name "antuitrin-G." They injected 2 cc. of this substance three times a week and report that no untoward results were noted at any time. The increase in height varied from 1 to $2\frac{9}{10}$ inches. These patients were from 7 to 18 years of age. They were under observation before treatment from four to six months, and under treatment with antuitrin-G from three to five months. These investigators found that the addition of thyroid extract was a valuable adjunct in the treatment. The improvement was indicated not only by increase in height but also by roentgen examination of the bones, which showed an advance in osseous development.

In the use of these remedies one should not be overasanguine as to results. The writer of the query is advised to read the editorial contained in The Journal, August 18, "Antihormones," which emphasizes that antihormones may be produced in the body by the administration of endocrine substances and indicates the advisability of utmost caution in their clinical use.

PREVENTION OF HEMORRHAGE IN CESAREAN OPERATION

To the Editor:—In doing a cesarean section, what medicine is usually injected to prevent uterine hemorrhage? I understand that solution of pituitary and ergot are usually employed. Should they be injected together? How long does it take for them to work ordinarily? Should they be injected into the uterus or subcutaneously or intramuscularly? If the solution of pituitary starts to act as the incision is started in the uterus is there any likelihood of its causing such fast or strong contraction of the uterine musculature that the uterus will tear by its own contraction? The work is being done under spinal anesthesia. Please omit name.

M.D., Texas.

Answer.—Obstetricians who employ solution of pituitary and ergot to prevent uterine hemorrhage in cases of cesarean section generally give 1 cc. of ergotamine tartrate, or Gynergen, hypodermically just before the operation is begun and 1 cc. of solution of pituitary immediately after the baby is extracted from the uterus. Both injections are usually given intramuscularly in the deltoid muscle. However, not infrequently the solution of pituitary is injected directly into the uterine musculature, a sterile needle being used, of course. This method produces much more prompt contractions of the uterus. Often the uterus becomes contracted and blanched within one minute after the injection. When the solution of pituitary is injected into the arm, the uterus usually contracts within two or three minutes. The general belief is that the effect of ergot does not become manifest for from fifteen to twenty minutes; hence this drug is given before the operation is begun.

Recently there has arisen doubt about the potency of hypodermic preparations of ergot, some investigators maintaining that such preparations have practically no effect on the uterus. There is, however, almost unanimity of opinion concerning the fact that fluidextract of ergot, as administered by mouth, has a definite, stimulating effect on the uterus. Hence ergot may be given by mouth before a cesarean section, especially if local anesthesia is to be used. If solution of pituitary is given before the baby is delivered, the uterus may contract so markedly that there will be difficulty in extracting the child. The uterus, however, will not tear unless the operator attempts to deliver the child forcibly.

Spinal anesthesia will not inhibit the effect of pituitary extract on the uterus. However, as has been pointed out by a number of observers, spinal anesthesia is much more hazardous for pregnant than for nonpregnant women. Whenever possible, direct infiltration anesthesia should be used instead of spinal anesthesia, because it is simple and much safer than spinal anesthesia.

SPINAL FLUID EXAMINATION IN SYPHILIS

To the Editor:—I should like to know the consensus on the interpretation of the spinal fluid examination in the different forms of syphilis with the presence and absence of the characteristic laboratory observations, including the blood Kahn and Wassermann tests. I am particularly interested in whether a diagnosis of dementia paralytica could be made on the finding of a paretic curve with a negative spinal Wassermann reaction, a positive blood Wassermann reaction, and normal cells, Ross Jones and Pandy. The diagnosis of dementia paralytica in this particular case was disputed, despite the fact that the clinical picture would well fit that of dementia paralytica. Kindly omit name.

M.D., Chicago.

Answer.—Spinal fluid changes may occur in the primary and secondary stages of syphilis but are most pronounced and of highest diagnostic value in the late stages of the disease.

In the latter, however, the blood Wassermann and Kahn tests may give positive reactions with no abnormal changes in the spinal fluid. However, just the reverse may occur with pronounced spinal fluid changes of pleocytosis, increase of protein, positive Wassermann reaction and a colloidal gold curve (usually of the zone II type) when the blood tests give negative reactions. Such usually occur in cases of asymptomatic neurosyphilis but constitute a very important reason for the routine examination of the spinal fluid in cases of chronic syphilis, and particularly before treatment is stopped, to prevent the regrettable mistake of undertreating the disease.

Unfortunately, the colloidal gold test is subject to error because of difficulties in the preparation of the reagent. In the case cited the spinal fluid gave a paretic curve (zone I) with a negative Wassermann reaction, normal cell count and no increase of protein. Under these conditions the question of probable dementia paralytica must be questioned, since in this

type of neurosyphilis the Wassermann reaction by an acceptable method is almost invariably positive along with pleocytosis and increase of protein. It would be hazardous to conclude that dementia paralytica is present on the basis of the colloidal gold reaction alone because of the chances of technical error referable to the reagent, which may precipitate if the gold is insufficiently "protected."

On the other hand the colloidal gold test with a proper reagent is of high diagnostic value, but curves of precipitation are associated with positive Wassermann reactions and pleocytosis in the majority of cases. Indeed, a paretic curve in association with positive blood and spinal fluid Wassermann reactions may be the earliest indications of impending dementia paralytica when the signs and symptoms of the disease are indefinite and uncertain.

STERILITY WITH ENDOCRINE DEFICIENCIES

To the Editor:—A woman, aged 29, married six years, apparently enjoys good health except for the following complaints: She is unable to become pregnant. The periods are irregular. Sometimes she misses one completely; they are of normal amount and duration. The patient's hair will not take a permanent wave (she tried four times in two years) since an operation for appendicitis about two years ago; it was normal to that time. There is occasional arthritis of the middle fingers with no evidence of focal infection except sinusitis at times. The patient is 5 feet 5 inches (165 cm.) tall and weighs 130 pounds (59 Kg.). Her habits are normal. The basal metabolic rate was plus 2 about eighteen months ago. Four tubal insufflation tests have been made in the past two years. The first test required higher than normal pressure, but the others were fairly normal. At the time of the appendectomy, a laparotomy was done and the pelvic organs were found to be normal. The tubes were traversed with a small probe, and iodized oil was injected into the fimbriated ends. The external genitalia are normal. Alkaline douches have been taken before intercourse. The husband's spermatozoa have been found to be virile. What part do you think the pituitary and the ovaries have to do with these complaints? Please omit name.

M.D., Illinois.

ANSWER.—A thorough and systematic investigation of both partners is indicated to determine the cause or causes of the apparent sterility. The history indicates several faults in the wife. A check-up of the husband may likewise reveal constitutional or endocrine causes for his share in the reproductive failure in spite of the finding of live spermatozoa.

In the wife a definite endocrine fault is suggested by the history of irregular menstruation, infertility, and the stringy condition of the hair. The latter probably relates to a thyroid gland deficiency, although the pituitary gland may be partly responsible. Lowered constitutional states may also cause changes in the texture and quality of the hair. The history of digital arthritis suggests a possible focus of infection, and the recurrent sinusitis may well be responsible for this condition. The same condition may adversely influence the general constitution and thus predispose to lowered fertility. The disturbed ovarian function is probably only secondary to the other endocrine gland derangements. The therapy indicated is: 1. Attention to the sinus and any other foci of infection that may be discovered. 2. Endocrine treatment; thyroid extract may be given in small doses even if the metabolism measures within the normal range. The condition of the hair will probably improve on thyroid therapy and the menstrual cycle may become regular. 3. General hygienic and tonic measures.

If the health level in both partners is raised and their constitutional states are improved, fertility in their mating may be established.

APPEARANCE OF HEART MURMUR AFTER INJECTION OF DIPHTHERIA TOXOID

To the Editor:—A boy, aged 9 months, was given one hypodermic injection of diphtheria toxoid (Lederle). Two able men had given him routine physical examinations previously, and he was examined at the time of the injection and nothing abnormal was found. Six months later at another routine examination he is found to have an apparent cardiac enlargement with a loud, rough mitral murmur. His mother states that neither previous to the injection nor since it has he had any type of infection, especially any infection of the upper respiratory tract, has "not missed a meal" and has not had any other symptom. Do you believe the toxoid is responsible here; if not, what else could be? Please omit name.

M.D., Connecticut.

ANSWER.—There is no evidence anywhere that diphtheria toxoid can produce a cardiac enlargement or murmur. Without any history of infection or any sign of illness from the time of the toxoid inoculation to the accidental finding of the cardiac signs, it can only be concluded that the condition had been present earlier. Cardiac murmurs are so common in infancy that the examiner frequently ignores them in the record even when he notices the sign on examination.

RECURRING HEMOLYTIC CRISES

To the Editor:—An American girl, aged 10 years, has intermittent attacks of anemia, occurring about every five or six months. She complains of "hurting all over" and marked weakness. Examination reveals a marked dyspnea, tachycardia and yellow skin. The hemoglobin (Tallqvist) is 16 per cent. The edge of the spleen extends almost to the crest of the ilium. The edge of the liver is at the umbilicus. The liver is tender. There is a hemic murmur in the heart. The coagulation time is normal. The red count is 250,000. The bleeding time is prolonged. The white count is 7,000, with 19 per cent small lymphocytes, 19 per cent large lymphocytes and 62 per cent polymorphonuclears. There is only a moderate anisocytosis, but the shape of the red cells includes tennis rackets. The history revealed that liver extract by mouth had revived the patient from these attacks for several years. I gave it intramuscularly and the child gradually showed improvement. After three or four days of improvement, hemorrhage began from the nose. This is the only place she has ever bled. The bleeding from the nose continued for two days and two nights, regardless of treatment (the father's blood was used intramuscularly and fibrinogen was administered). No platelet count has been made. Repeated stool examinations show no ova. No infection or allergic evidence is found. Between these attacks the patient has a red count of about 1,000,000, the color index is from 0.9 to 1.1, and she is up and out with the children. My impression is that the child has an idiopathic thrombocytopenic purpura haemorrhagica. Please give me your opinion of this case. What do you think of splenectomy? What is the chance of cure with and without splenectomy? How high should the red count and hemoglobin be before the operation is performed? Please furnish other suggestions as regards treatment and operation.

JOHN D. CAMPBELL, M.D., Duncan, Okla.

ANSWER.—It is possible that this patient has severe, recurring, hemolytic crises. This suspicion leads to a request for an estimation of the percentage of reticulated erythrocytes and of the fragility of the erythrocytes. If the percentage of reticulated erythrocytes is abnormally high and the fragility of the erythrocytes is increased, hemolytic icterus would almost certainly be the correct diagnosis and, in the event of exclusion of other diagnoses, splenectomy would be indicated. The question of thrombocytopenic purpura is raised in the query. The physician's notes do not indicate that clinically the features of hemorrhagic purpura have been consistently present, and there is no note concerning retractility of clot or platelet count. It is not indicated in the notes whether or not syphilis has been excluded. It would also be well to have roentgenograms of the skull and of the long bones, particularly to exclude the possible existence of Gaucher's disease or some other type of lipoid histiocytosis. The erythrocyte count of 250,000 during attacks and a count of 1,000,000 when the child is up and about with other children are most likely clerical errors; if the count of 250,000 is correct it is one of the lowest on record. The question of treatment would depend entirely on accurate diagnosis. In the event of splenectomy it is desirable to have the erythrocyte count more than 3,000,000 before the operation, and splenectomy should not be done during an acute crisis.

VACCINATION OF ASTHMATIC PATIENTS

To the Editor:—Will you please tell me what, if any, variation of reaction one gets in vaccinating asthmatic patients against smallpox? An instance came to my attention of a very severe reaction in a person who had asthma. Is it liable to produce more severe local reaction or set up asthmatic attacks? Kindly omit name.

M.D., Michigan.

ANSWER.—The reactions that may occur with smallpox vaccination in persons with asthma are similar to those that may occur with any foreign protein inoculation in any allergic individual. There is a tendency for nonspecific proteins to cause a more marked local reaction in allergic individuals. This is by no means constant nor does it occur in the majority. There is a similar tendency to produce a more severe systemic disturbance in allergic persons—a higher temperature and more marked malaise. This is probably due to the fact that the temperature-regulating mechanism in allergic persons is as a whole more easily disturbed. Frequently one sees, for example, high temperatures with a slight rhinitis, constipation or other minor disturbances in asthmatic children.

It may be possible to precipitate an attack of asthma by nonspecific means acting as a disturbing factor in overthrowing the allergic equilibrium. The reaction from smallpox vaccination may be such a factor. However, this is not very likely to occur. The more likely possibility is that the fever resulting from the vaccination may cause an actual temporary relief of the asthma when the latter is chronic. The latter effect of fever, with or without infection, on the course of asthma and other allergic conditions is a frequent clinical observation.

It is possible that the patient may be sensitive to the beef protein contained in the vaccine virus. It is not likely, however, that there would be sufficient absorption from scratches to produce an allergic reaction. Such a response, if it should occur, would take place within a few minutes or an hour or two.

ENURESIS AFTER SPINAL INJURY

To the Editor:—I have a patient, aged 20, who in an accident received a crushing fracture of the third lumbar vertebra with involvement of the lateral arches, also a fracture of the transverse processes of the fourth lumbar vertebra. There was no gross injury of the spinal cord. The reflexes are normal. Sensory reactions as well as muscle reactions and use of the limbs is normal. There is no residual urine. There is no difficulty with urination during the daytime. There is no bladder infection. Blood tests are negative. Following the injury there was no difficulty in any way with injury or with the bladder and urine, but there has now developed bed wetting. The patient had never had any such previous trouble since childhood. The sympathetic fibers that run through the sympathetic chain go through the third, fourth and fifth lumbar roots. Could the fibers that go to the bladder have been injured at the time of the injury or could they be involved in callus formation at the present time? Stimulation of these sympathetic fibers causes increase of tonus of the bladder sphincter. Could there be a degenerative involvement of these fibers with loss of tone of bladder sphincter resulting in bed wetting? If not, just what would anatomically be the basis for this symptom, which is most distressing to the patient? Please omit name and locality.

M.D., Missouri.

ANSWER.—The sympathetic fibers innervating the bladder in man arise somewhere between the ninth dorsal and the fourth lumbar vertebrae. The exact origin is not known. They are motor to the ureterovesicular orifices, the trigonal musculature and the internal sphincter, and inhibitory to the detrusor muscles of the bladder. It is not likely that these fibers were injured at the time of the accident, since the difficulty with the function of the bladder came on much later; but they may be now involved in the formation of the callus.

The bed wetting from which the patient suffers is probably due to weakening of the internal sphincter. It is quite possible that there may be connective tissue adhesions which involve the nerves within the spinal canal. One might get some evidence by means of Queckenstedt's test or by injection of iodized oil into the spinal canal.

SALT IN HYPERTENSION AND IN PREGNANCY

To the Editor:—In answer to a query by a physician in Iowa on pregnancy and hypertension, published on page 1011 of the Sept. 29, 1934, issue of THE JOURNAL, among other things it is stated that "it is advisable to eliminate all salt from the food." The patient described by the physician who asks the question has a systolic blood pressure varying between 160 to 176 mm. and has no edema. I should like to know why the n...n who wrote the answer proscribed salt. My recollection is that the work of the Fishbergs as well as that of others has definitely proved that sodium chloride plays no part in hypertension.

ALBERT W. HOLMAN, M.D., Portland, Ore.

ANSWER.—The experimental results obtained by V. J. Harding and H. B. Van Wyck (*J. Obst. & Gynec. Brit. Emp.* **33**:17, 1926) led them to conclude that "in the treatment of pre-eclampsia there is only one pertinent dietetic factor. It is the presence or absence of salt." Later (*Canad. M. A. J.* **24**:635 [May] 1931) the same authors expressed the opinion that a high intake of salt, taken at the right moment, in a developing toxemia will produce an albuminuria, an increased blood pressure and convulsions in a short time. They therefore consider salt restriction a necessary part of prenatal care.

It is true that in recent years a great deal of doubt has been cast on salt as a harmful substance in cases of hypertension and the toxemias of pregnancy. In spite of this there are still adherents of a strictly salt-free diet in cases of hypertension (Allen, F. M., and Sherrill, J. N.: *J. Metab. Research* **2**:429, 1922, and Blaisdell, E. A.: *Boston M. & S. J.* **196**:808 [May 19] 1927). Most authorities agree that an excess of salt may be injurious. Probably the safest procedure is to permit patients who have hypertension to eat food that contains the customary amount of salt added during cooking. However, the patient should not add more salt when the food is eaten.

GLASSITE AS INDUSTRIAL HAZARD

To the Editor:—I should like to know the composition of the abrasive "Glassite," which is used in glass polishing, and whether its use constitutes a hazard of silicosis. Please omit name.

M.D., Ohio.

ANSWER.—In Thomas's Register of American Manufacturers, in the section headed "Leading Trade Marks," is the following entry: "Glassite, Bone Dry Black Rouge, James H. Rhodes & Co., 153 W. Austin Ave., Chicago, Ill. Black rouge. Black rouge is ferrosoferric oxide (black iron oxide) having the formula $Fe_3O_4H_2O$. This substance is widely used in glass polishing but is less used than the common red oxide of iron. The black oxide is less abrasive than the red oxide and is employed for scratch polishing and wherever a very fine finish is required. Black rouge is not an industrial toxic agent. Gross exposure causes practically no changes in the lungs. Very certainly it may not be classed as similar to silica in its action. Any dusty lung disease produced should be termed 'siderosis,' but so-called cases of siderosis are often properly attributable to silica or silicates associated with iron ores. At this time the belief is that black rouge may not become the source of any direct pulmonary condition other than a minor 'increased noncharacteristic fibrosis.'"

RENAL TUBERCULOSIS

To the Editor:—A woman, aged 26, a college graduate and athletically inclined, married one year, has been complaining of dysuria for the past two years. Cystoscopy has been done repeatedly by prominent urologists and she has been placed on various urinary antiseptics to no avail. Oil of santal interferes with her digestion within twenty-four hours. The attacks last from several days to several weeks with relief for only three or four days at a time. On cystoscopy three months ago I found a moderately inflamed trigon and urethra. The left ureter was readily catheterized. A No. 6 catheter encountered an obstruction in the right ureter about 5 cm. above the orifice but passed with some slight difficulty. Kidney function on both sides was normal. The urine from the right kidney pelvis showed several pus cells. The following week cystoscopy was repeated by a urologist in another city who had been treating her previously. He was able to pass a No. 9 catheter, apparently with relative ease. She then had relief for more than a month. This physician has suggested pregnancy on the supposition that the resultant pelvic congestion may cure the condition. Roentgenograms show a spasmlike stricture of moderate degree at the region of the obstruction. Physical examination is essentially negative. She has never had any inflammatory process in the abdomen or the pelvis. The patient is very desirous of having a child. Would you advise the risk of pregnancy? Is it true that pregnancy occasionally affords relief in such a condition? Have you any suggestions to offer other than repeated ureteral dilations? Incidentally, bladder irrigations with silver nitrate, potassium permanganate and mild silver protein have been tried with relief only during the time during which she was receiving treatment. Please omit name.

M.D., New York.

ANSWER.—The presence of pus cells in one kidney in a woman of 26 who complains of dysuria leads one to suspect that she might have tuberculosis of the kidney. Therefore it is in order to make repeated examinations of catheterized bladder specimens for the presence of tubercle bacilli. If they cannot be demonstrated in smear it might be well to inoculate several guinea-pigs. If pyelograms have been made, they should be studied carefully for the possibility of renal tuberculosis. It might be a good plan to have some plain roentgenograms made to rule out stone.

If dilation has been done with No. 9 bougies or catheters, and if the trouble is due to a ureteral stricture, this amount of dilation should relieve the symptoms. Therefore I would discontinue further ureteral dilation and bladder treatments.

It may be possible that the symptoms are due to a chronic urethritis, and it may be a good plan to strip out the urethra for the presence of pus and to search for the presence of infection in Skene's glands.

Pregnancy probably would not relieve the patient of her symptoms. If the patient does not have renal tuberculosis, there would seem to be no reason why she should not become pregnant.

DIFFERENTIAL DIAGNOSIS IN ERYTHEMA MULTIFORME

To the Editor:—A man, aged 60, of Italian ancestry, noticed a small bluish spot on the dorsum of the proximal phalanx of the left little finger. This gradually spread until it advanced across the back of the hand and up the arm. The skin seems to separate, leaving a granulated surface dotted with islands of unharmed skin. Healing takes place without scarring. He reports to me that he has had five previous attacks at intervals of about two years. His physical examination and blood chemistry are negative. What is the diagnosis and what would you suggest in the way of treatment? Please omit name.

M.D., Ohio.

ANSWER.—The periodicity of the attacks and the apparently extensive destruction of the skin, which, however, proves to be too superficial a process to cause scarring, suggests erythema multiforme, which causes just such apparently gangrenous conditions. They are so superficial, however, that scarring never results. Erythema multiforme is typically bilateral and symmetrical. It is supposed by some to be caused by showers of bacilli producing emboli in the small vessels of the skin. It is conceivable that such a process might be active in the arteries of one arm. The vascular supply should be studied carefully. If possible, the patient should be seen by a dermatologist during an attack.

Erythema multiforme-like eruptions are sometimes caused by drugs, quinine, iodine, bromine, and some of the coal tar derivatives.

Recurrent erysipelas might be considered, but no bluish spot or deep erosions are apt to be seen in this disease. No diagnosis can be made without a careful study of the case, which is evidently a rare one.

Medical Examinations and Licensure

COMING EXAMINATIONS

ALASKA: Juneau, March 5. Sec., Dr. W. W. Council, Juneau.

AMERICAN BOARD OF DERMATOLOGY AND SYPHILOLOGY: *Written (Group B candidates).* The examination will be held in various cities throughout the country, April 29. *Oral (Group A and Group B candidates).* New York, June 10. Sec., Dr. C. Guy Lane, 416 Marlborough St., Boston.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Written (Group B candidates).* The examination will be held in various cities of the United States and Canada, March 23. *Final oral and clinical examination (Group A and Group B candidates).* Atlantic City, N. J., June 10-11. Group B application lists close Feb. 23 and Group A application lists close May 10. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: Philadelphia, June 8, and New York, June 10. *Application must be filed at least sixty days prior to date of examination.* Sec., Dr. William H. Wilder, 122 S. Michigan Blvd., Chicago.

AMERICAN BOARD OF OTOLARYNGOLOGY: New York, June 8. Sec., Dr. W. P. Wherry, 1500 Medical Arts Bldg., Omaha.

AMERICAN BOARD OF PEDIATRICS: Atlantic City, N. J., June 10, and St. Louis, Nov. 19. Sec., Dr. C. A. Aldrich, 723 Elm St., Winnetka, Ill.

ARIZONA: *Basic Science.* Tucson, March 19. Sec., Dr. Robert L. Nugent, Science Hall, University of Arizona, Tucson.

CALIFORNIA: *Reciprocity.* Los Angeles, March 13. Sec., Dr. Charles B. Pinkham, 420 State Office Building, Sacramento.

CONNECTICUT: *Regular.* Hartford, March 12-13. *Endorsement.* Hartford, March 26. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic.* March 12. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

MAINE: Portland, March 12-13. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton Jr., 192 State St., Portland.

MASSACHUSETTS: Boston, March 12-14. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 144 State House, Boston.

NATIONAL BOARD OF MEDICAL EXAMINERS: *Parts I and II.* The examinations will be held in medical centers where there are five or more candidates, Feb. 13-15. Ex. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia.

NEW HAMPSHIRE: Concord, March 14-15. Sec., Board of Registration in Medicine, Dr. Charles Duncan, State House, Concord.

OKLAHOMA: Oklahoma City, March 12-13. Sec., Dr. J. M. Byrum, Mammoth Bldg., Shawnee.

PUERTO RICO: San Juan, March 5. Act. Sec., Dr. Ramón M. Suarez, Box 536, San Juan.

VERMONT: Burlington, Feb. 13-15. Sec., Board of Medical Registration, Dr. W. Scott Nay, Underhill.

WEST VIRGINIA: Charleston, March 18. State Health Commissioner, Dr. Arthur E. McClue, Charleston.

WISCONSIN: *Basic Science.* Madison, March 16. Sec., Prof. Robert N. Bauer, 3414 W. Wisconsin Ave., Milwaukee.

Arizona October Report

Dr. J. H. Patterson, secretary, Arizona State Board of Medical Examiners, reports the written examination held in Phoenix, Oct. 2-3, 1934. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Two candidates were examined, both of whom passed. Four physicians were licensed by reciprocity. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
George Washington University School of Medicine		(1933)	85.8
Northwestern University Medical School		(1934)	85.2

School	LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
School of Medicine of the Division of the Biological Sciences, University of Chicago		(1932)	Illinois
St. Louis University School of Medicine		(1926)	Utah
University of Tennessee College of Medicine		(1915)	Oklahoma
Baylor University College of Medicine		(1931)	Texas

Rhode Island October Examination

Dr. Lester A. Round, director, Rhode Island Public Health Commission, reports the written examination held in Providence, Oct. 4-5, 1934. The examination covered 7 subjects and included 70 questions. An average of 80 per cent was required to pass. Twelve candidates were examined, 10 of whom passed and 2 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Georgetown University School of Medicine		(1934)	84,* 89*
Boston University School of Medicine		(1932) (1934)	82.1, 82,* 84.7*
Tufts College Medical School		(1933)	84.5, 88.1
Hahnemann Med. College and Hospital of Philadelphia		(1934)	91.1*
Temple University School of Medicine		(1933)	85.4
University of Toronto Faculty of Medicine		(1933)	89.5

School	FAILED	Year Grad.	Per Cent
Tufts College Medical School		(1934)	76.5
Universidade de Lisboa Faculdade de Medicina		(1932)	72

* License withheld pending completion of internship.

Illinois October Examination

Mr. Eugene R. Schwartz, superintendent of registration, Illinois Department of Registration and Education, reports the written and oral examination held in Chicago, Oct. 16-18, 1934. The examination covered 10 subjects and included 100 questions. An average of 75 per cent was required to pass. Sixty-five candidates were examined, 62 of whom passed and 3 failed. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Chicago Medical School		(1934)	77,* 78,* 78, 81, 86
Loyola University School of Medicine		(1934)	77, 82, 86*
Northwestern University Medical School		(1925) (1934)	81, 81, 82,* 82, 84,* 84,* 84,* 84, 85,* 85, 86, 86, 87,* 88
Rush Medical College		(1930) (1932)	77, 84,* (1934) 79, 79, 82,* 82, 83, 83, 83, 84, 85,* 85,* 85
Sch. of Med. of the Division of the Biological Sciences		(1933)	78*
University of Illinois College of Medicine		(1934)	78,* 78, 80, 81,* 82, 83, 83, 84,* 84, 85,* 85,* 85, 85, 86,* 86, 86
Indiana University School of Medicine		(1921)	82
Harvard University Medical School		(1931)	85
Tufts College Medical School		(1933)	81*
Hahnemann Med. College and Hospital of Philadelphia		(1932)	82*
University of Wisconsin Medical School		(1932) 80,* (1933)	82*
University of Manitoba Faculty of Medicine		(1934)	77*
Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany		(1931)	77†
Schlesische Friedrich-Wilhelms-Universität Medizinische Fakultat, Breslau, Prussia, Germany		(1927)	79†

School	FAILED	Year Grad.	Number Failed
Chicago Medical School		(1932), (1933)	2
Meharry Medical College		(1916)	1

Thirty physicians passed the practical examination for reciprocity and endorsement applicants. The following schools were represented:

School	PASSED	Year Grad.	Reciprocity with
Northwestern University Medical School		(1928) (1930)*	Wisconsin, Arizona, Texas
University of Illinois College of Medicine		(1933)*	Missouri
State University of Iowa College of Medicine		(1932)*	Iowa
University of Louisville School of Medicine		(1933)	Kentucky
University of Maryland School of Medicine and College of Physicians and Surgeons		(1928)	Maryland
Detroit College of Medicine and Surgery		(1931)	Michigan
Univ. of Michigan Dept. of Medicine and Surgery		(1914)*	Michigan
University of Minnesota Medical School		(1927),* (1934)	Minnesota
Washington Univ. School of Med.		(1932),* (1932), (1933, 2)	Missouri
University of Nebraska College of Medicine		(1933),* (1933)	Nebraska
University of Cincinnati College of Medicine		(1934)	Ohio
Jefferson Medical College of Philadelphia		(1926)*	Ohio
University of Tennessee College of Medicine		(1931)*	Tennessee
Medical College of Virginia		(1933)	Virginia
University of Wisconsin Medical School		(1928), (1930)*	Wisconsin
McGill University Faculty of Medicine		(1928)	Maryland

School	PASSED	Year Grad.	Endorsement of
Northwestern University Medical School		(1933)*	N. B. M. Ex.
Rush Medical College		(1933), (1934)	N. B. M. Ex.
University of Illinois College of Medicine		(1931)	N. B. M. Ex.
Jefferson Medical College of Philadelphia		(1917)	N. B. M. Ex.
University of Pennsylvania School of Medicine		(1928)*	N. B. M. Ex.

* License withheld pending payment of fee.
† Verification of graduation in process.

Hawaii October Examination

Dr. James A. Morgan, secretary, Board of Medical Examiners, reports the oral and written examination held in Honolulu, Oct. 8-11, 1934. The examination covered 10 subjects and included 55 questions. An average of 75 per cent was required to pass. Five candidates were examined, 2 of whom passed and 3 failed. Three physicians were licensed by endorsement after an oral examination. The following schools were represented:

School	PASSED	Year Grad.	Per Cent
Northwestern University Medical School		(1934)	84*
Jefferson Medical College of Philadelphia		(1934)	81†

School	FAILED	Year Grad.	Per Cent
Loyola University School of Medicine		(1934)	77‡
Washington University School of Medicine		(1932)	81‡
University of Oregon Medical School		(1934)	80‡

School	LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
College of Medical Evangelists		(1934, 2)	N. B. M. Ex.
Northwestern University Medical School		(1932)	N. B. M. Ex.

* This applicant has received an M.B. degree and will receive an M.D. degree and Hawaii license on completion of internship.
† License withheld pending completion of internship.
‡ Failed in more than three subjects.

Book Notices

Accepted Dental Remedies Containing a List of Official Drugs Selected to Promote a Rational Dental Materia Medica and Descriptions of Acceptable Nonofficial Articles, 1934. Council on Dental Therapeutics. Cloth. Price, $1. Pp. 204. Chicago: American Dental Association, 1934.

This book should be as valuable to the dental profession as are its prototypes, Useful Drugs and New and Nonofficial Remedies, to the medical profession. In format and general scope it resembles the former publication, but in that it lists and describes nonofficial remedies proposed for use by dentists it resembles the latter. The typography is excellent.

The names appearing in the list of members of the Council on Dental Therapeutics as well as the text of the rules governing the admission of articles assure both the scientific background and the practical soundness of the council's actions and consequently of the contents of this book. The official preparations included represent such an admirably short and selective materia medica as will be of most usefulness to the busy dental practitioner. The point of view of the dentist has been constantly and effectively kept in mind. It is planned to revise the list of drugs annually.

In a book such as this, sponsored by the dental association, both the professional and the lay reader will be much interested in the section devoted to dentifrices. The well informed will highly approve the sound and sane presentation of the subject. The council holds that "the sole function of a dentifrice is to aid in keeping the teeth clean by the removal of loose food débris by the mechanical use of the tooth brush." This offers small encouragement to manufacturers who would "protect the danger line," "avoid pink tooth brush" or propagate the many other fantastic claims advanced to make a "tooth conscious" public justify their advertising appropriations. The book lists some sixteen accepted preparations of this class, giving the composition and permitted claims for each. Among these appear the names of only two widely advertised products, "Iodent Tooth Paste No. I" and "Iodent Tooth Paste No. II." With the descriptions of these appears a statment by the firm to the effect that no therapeutic claims will be made until sound evidence is available to warrant them.

The book contains descriptions of various accepted cod liver oils and related preparations. In the general discussion under which these are listed, the council takes a wisely conservative stand on the dental claims that may be made for such products. This is shown by the following statement:

> Cod liver oil is considered to be among the medicinal foods which, because of their vitamin content, apparently have a beneficial effect on the development of teeth and aid in the prophylaxis against dental caries. The exact rôle that vitamin D plays in such prophylaxis is, at present, not clearly understood (Diet and the Teeth, Reports of the Council, J. A. D. A. 19:1843 [Oct.] 1932).

The dosages given are based on the curative properties against experimental rickets; in the absence of the available data no dosage is given for prophylaxis against caries or other dental diseases.

The bibliographic indexes at the end of the book give an idea of the scope and volume of the work done by the council on accepted products and subjects of general interest to dentists since 1930. Some ninety regular reports of the council and some twenty-five special reports, including those of the American Dental Association Bureau of Chemistry, have been published in the *Journal of the American Dental Association*. The bureau's report on mouth washes shows agreement between the Council on Dental Therapeutics and the Council on Pharmacy and Chemistry in skepticism concerning the much vaunted efficacy of these preparations.

The book has a well prepared section on symptoms and treatment of acute poisoning, a list of recorded solubilities, helpful tables of weights and measures, and a therapeutic index based on that given in the latest edition of Cushny's Pharmacology and Therapeutics. There is an adequate index to the text of the book itself.

The American Dental Association is to be congratulated on this new step in the fostering of rational therapeutics, for which it is indebted to its excellent Council on Dental Therapeutics; it is to be hoped that the book will receive from dental practitioners the attention—and support—it so well deserves.

Krebs und Vererbung. Von Prof. Dr. Hans R. Schinz und Dr. Franz Buschke. Paper. Price, 21 marks. Pp. 280, with 100 illustrations. Leipzig: Georg Thieme, 1935.

This is a critical review of much of the present-day literature on the influence of heredity on the occurrence of cancer both in man and in experimental animals. After a brief presentation of the principles of heredity in the light of modern work, the literature on the genetics of spontaneous tumors in laboratory animals is reviewed. From the evidence now available the authors conclude that "at present the assumption of a simple recessive factor for the adenocarcinoma of the mamma of the mouse is most easily harmonized with the observed facts," which conclusion is in agreement with the views advanced in this country by Maud Slye. They further state, however, "But we must be clear that this conclusion is valid only for this one tumor" and cannot be applied indiscriminately to all tumors. They then consider some of the evidence on the genetics of human tumors, of transplanted tumors in animals, and of the tumors produced by chemical or parasitic stimulation of tissues. As to the relative importance of hereditary and environmental influences in the production, the evidence indicates that this varies greatly with different sorts of tumors; thus, there are three great groups: 1. Cancers almost entirely dependent on the hereditary background; e. g., retinal gliomas. 2. Cancers in which the exciting stimulus is much more important than the heredity, as with superficial cancers resulting from protracted stimulation by tar, x-rays, and so on; but even here the hereditary background is a primary factor in determining at least the time required to produce such cancers. 3. The majority of human cancers, which seem to lie between these two groups, the hereditary background being essential and the exciting agent often being a physiologic stimulus (e. g., the influence of endocrine stimulation of mammary gland cancers). Apparently, with glandular cancers the heredity factor seems to be more important than with squamous cell carcinomas. While active workers in the field of cancer etiology and genetics will probably take exception to many statements and deductions made by these authors, as they do with one another's utterances in this new and unstabilized field, this publication gives a good general survey of an important subject—perhaps the best now available. An extensive bibliography is appended.

Clinical Pathology of the Jaws with a Histologic and Roentgen Study of Practical Cases. By Kurt H. Thoma, D.M.D., Charles A. Brackett Professor of Oral Pathology in Harvard University. Cloth. Price, $9. Pp. 643, with 423 illustrations. Springfield, Illinois, and Baltimore: Charles C. Thomas, 1934.

This book contains a wealth of material that is not available anywhere else. The author has had an unusual opportunity to study lesions of the jaw bones from the point of view of the clinic and the laboratory and has been diligent and faithful in the accumulation of the records of this experience, such as case histories, photographs and histologic slides. Of the illustrations, 189 are reproductions of roentgenograms, more than 100 are prints of photomicrographs of histologic preparations, and the remainder are photographs and drawings chiefly of the gross aspects of jaw disease. There are 171 case histories, of which eighty-three concern tumors, twenty-three deal with cysts, and the remainder have to do with all other conditions. Each of the chapters has a generous bibliography, especially those on malformations, endocrine disturbances and tumors. There are two indexes, one of the conventional type, which is quite adequate, and one for the case histories. Because of the general excellence of the book, minor defects become unduly conspicuous. Most of the illustrations are without legends, so that one has to refer to the text for names and explanations; the task of coordinating reading and study of the illustrations is thereby made unduly laborious. All of the illustrations except many of the photomicrographs attain a high standard of excellence, partly because of technical superiority in reproduction and the high quality of the paper used. Since the interpretation of even an excellent histologic illustration is generally difficult for the average reader, there is little excuse for the use of inferior reproductions of tissue sections. The statement on page 140 that 75 per cent of the infections of the maxillary sinus are secondary to infections of the teeth should be questioned, as it seems too high. The failure to refer to Gilmer's work on jaw fractures and to Partsch's con-

tribution to the treatment of jaw cysts should be noted. For a first edition there are relatively few minor errors in printing and proofreading. This text is highly recommended to all those interested in diseases of the jaws, including medical and dental students, teachers and clinicians.

Über Carcinome, Sarcome und Lymphomatosis infiltrans bei weissen Mäusen: Versuche menschlichen Cancer auf Versuchstiere zu Übertragen. Von Johs. V. Andersen. Mit einer englischen und dänischen Zusammenfassung. Paper. Pp. 143, with illustrations. Copenhagen: Levin & Munksgaard, 1934.

For many years, investigators of cancer have endeavored to transfer neoplasms from one species to another by grafting. Recently the German investigators Keysser and Heidenhain stated that they were able to transfer human cancer to mice. While of no practical interest, except in arousing fears of the layman that he may catch cancer from laboratory animals, these statements have considerable biologic importance. Andersen has repeated all this work on a large scale and has found that it is almost certain that the tumors which Keysser and Heidenhain observed in their mice were spontaneous mouse tumors and not transplanted neoplasms derived from the human tumors which they had inoculated into their animals. The care with which Andersen's work is done, the accurate statistical analysis of the experimental material and the admirable photomicrographic reproductions of the tumors found will render unnecessary any future repetition of such experiments.

Questions cliniques d'actualité. 4e série. Par MM. Armand Delille et autres. Leçons professées à charité service du Professeur Sergent. Paper. Price, 45 francs. Pp. 280, with 53 illustrations. Paris: Masson & Cie, 1934.

The fourth volume of clinical discussions presented at the Hôpital de la Charité, Paris, France, covers the discussion of a variety of clinical and related problems by eminent French clinicians. The character and scope of these lectures varies from the empirical to the philosophical, as is illustrated by the following titles: the principal forms of onset and diagnosis of pulmonary tuberculosis in the child; pneumothorax in various clinical types of pulmonary tuberculosis; the pseudolithiasis form of carcinoma of the ampulla of Vater; a new technic for the treatment of lung abscess; dissociated symptoms of hypothyroidism in the child; the treatment of arterial obstruction in the extremities; acute primary infectious purpura; the mean arterial pressure and its importance; the danger of simple explanations in biology and medicine; a case of malignant granulomatosis with a mediastinal syndrome; periarteritis nodosum; clinical and anatomic studies of disseminated sclerosis; the general and therapeutic principles of bacteriophage; hyperpyrexia in nurslings; diaphragmatic hernia; some clinical considerations of the phrenic nerve; spirochetal meningitis; the onset of acquired characteristics. The character of the subjects presented by such representative authors offers a good index of French thought in clinical medicine and should therefore interest the general reader in medicine. This volume, however, is of little value as a general reference work on the various subjects discussed because of the lack of references to the international literature and the point of view, which is limited to the French school.

Recent Advances in Ophthalmology. By Sir Stewart Duke-Elder, M.A., D.Sc., Ph.D., Ophthalmic Surgeon and Lecturer in Ophthalmology, St. George's Hospital, London. Third edition. Cloth. Price, $4. Pp. 434, with 153 illustrations. Philadelphia: P. Blakiston's Son & Company, 1934.

In the present edition the author follows the general outline of the previous work but omits the first four chapters of the second edition on the nature of light, physiologic optics, embryology and methods of diagnosis. He has divided his previous chapter on physiology into separate and more comprehensive ones on vascular circulation, intra-ocular fluids, intra-ocular pressure, the vitreous body and the effect of drugs on the eye, bringing these subjects down to date. The last mentioned chapter is an excellent review of the action of the drugs commonly used in study and therapy in ophthalmology. The second edition was chiefly concerned with glaucoma, cataract and neurology. In this edition the latter is omitted and the first two subjects are enlarged on. In the second part, on diseases of the eye, the author reviews intra-ocular infections, ocular pigment and intra-ocular tumors, disease of the conjunctiva, cornea and retina, and sympathetic ophthalmia. In discussing sympathetic ophthalmitis he mentions but takes little stock in Meller's contention that the disease is due to the tubercle bacillus. The chapter on retinal detachment is especially good in that it reviews the best work on this subject, gives the technic of the various operations accompanied by the author's own illustrations, and compares the results of the various methods. The discussion of cataract has been enlarged to contain newer knowledge of the metabolism and chemistry of the lens, as well as the electrodiaphake method for extraction introduced by Lacarrere. He also gives Sinclair's tables showing the visual results and complications in a series of 257 intracapsular extractions. The book is well written and illustrated, is a handy reference volume, and may be highly recommended for the student and practitioner.

A Text-Book of Pharmacology and Therapeutics or the Action of Drugs in Health and Disease. By Arthur R. Cushny. Tenth edition revised by C. W. Edmunds, A.B., M.D., Professor of Materia Medica and Therapeutics in the University of Michigan, Ann Arbor, Mich., and J. A. Gunn, M.A., M.D., D.Sc., Professor of Pharmacology in the University of Oxford, Oxford, England. Cloth. Price, $6.50. Pp. 786, with 75 illustrations. Philadelphia: Lea & Febiger, 1934.

This textbook has again been revised by the same pharmacologists who made the first revision following Dr. Cushny's death. They pay tribute to the original author with a biographic sketch, which replaces his preface to the eighth edition. The present edition brings the text into accord with the British Pharmacopeia of 1932, just as the ninth edition complied with the Pharmacopeia of the United States, tenth revision. This procedure results in the text being of use to both English and American students. There is a new section dealing with the liver and stomach preparations used in the treatment of primary anemias. The section on vitamins is elaborated: Carotene is included in the discussion of vitamin A and the division of vitamin B into B_1 and B_2 (G). There is additional material on iron and its compounds, more especially as to its administration. The section on bismuth is extended to include further material on its use in syphilis. There is a new section under hypnotics, which deals with the older and the newer barbiturates. The subject of digitalis has been revised in the light of the latest developments in its chemistry. The paragraphs on therapeutic uses immediately follow those on pharmacologic action instead of the lists of preparations being interposed as in the previous editions. There are over forty additional pages and two additional illustrations. The book is an excellent, modern textbook and reference work on the subject of pharmacology and therapeutics.

Opuscula selecta Neerlandicorum de arte medica. Fasciculus duodecimus quem curatores miscellaneorum quae vocantur Nederlandsch Tijdschrift voor Geneeskunde collegerunt et ediderunt Amstelodami Sumptibus Societatis. Varii auctores de symphysiotomia. Cloth. Pp. 383, with illustrations. Amsterdam, 1934.

This volume reprints in Dutch thirteen articles by Dutch physicians on symphysiotomy, published originally between 1771 and 1831. There is an introduction of thirty-two pages, and occasional comments appear by Dr. F. M. G. de Feyfer, who has made a special study of symphysiotomy in Holland up to 1840. Some of the articles are illustrated and there are five portraits. The book will be of great interest to students of the history of obstetrics.

The Hospital Yearbook: A Reference Book on Planning, Equipment, Administration and Purchasing. Thirteenth edition. Cloth. Price, $2.50. Pp. 543. Chicago: The Modern Hospital Publishing Company, Inc., 1934.

The planning and administration of a modern hospital involve more details than any one man can master alone, be he physician, architect, trustee or superintendent. The Hospital Yearbook presents a collection of information representing the contributions of a score or more of experienced hospital executives, architects and consultants. The first 200 pages consist mainly of concentrated check lists covering every conceivable detail in planning for ward patients and private patients; surgical facilities for the general hospital; the outpatient department; the maternity, children's, tuberculosis and psychopathic departments for the general hospital; contagious wards for the general hospital; laboratories; x-ray department; physical therapy facilities; hospital laundries; hospital kitchens, and the nurses' home. It is not assumed that any hospital

would include in its plans everything that is suggested. These lists are indispensable in the selection of proper equipment, devices, supplies, materials and layout. Following the planning section are articles on small hospitals, engineering, economics, contracting, modernizing, cost analysis, fire protection, air conditioning, equipment purchasing and supply lists. The administration section presents model articles of incorporation and by-laws, check lists for trustees, duties of the superintendent, major department heads and repair department. These are followed by condensed articles by qualified writers on noise, accidents, publicity, collections, accounting, costs, depreciation, insurance and numerous similar topics of everyday concern to the superintendent. The book is regarded as a valuable supplement to any textbook on hospital management and is a commendable start toward a compendium of standard reliable hospital information.

Endogene Faktoren in der Tumorgenese und der heutige Stand der Versuche einer biologischen Therapie. Von Professor Dr. G. Fichera, direttore generale dell'Istituto nazionale Vittorio Emanuele III per lo studio e la cura del cancro, Milano. Autorisierte Übersetzung aus dem italienischen. Paper. Price, 7.50 marks. Pp. 83, with 105 illustrations. Berlin: Julius Springer, 1934.

The basis of this monograph is the possibility that extracts of certain organs, particularly the spleen, lymph nodes and marrow, may be of benefit in the treatment of malignant tumors. The author believes that the clinical trial of such extracts is desirable. The experimental and other data on which the method is founded are presented.

Medicolegal

Workmen's Compensation Acts: Alleged Refusal of Employee to Submit to Medical Treatment.—In the course of his employment, on December 23, Haill ran a file in his hand. A clerk of the employer, who had charge of the employer's first aid station, washed the wound, applied certain preparations, and rendered "medical attention" to the employee daily for the succeeding three days. Until January 2, the workman's wife bathed his hand every evening in hot water in which she put "some sort of antiseptic." The hand seemed to be improving and, according to lay testimony, was healed from the outside. On January 2, however, there was a swelling and the workman went to a physician. On January 4, a fever developed and he was taken to a hospital, where he died January 7 from septicemia. His widow was awarded compensation by the workmen's compensation commission. The employer then appealed to the St. Louis circuit court, contending that the workman had unreasonably refused medical treatment. To sustain that contention, he relied on the testimony of the clerk in charge of the plant's first aid station and of the plant foreman that they had suggested to the workman on several occasions that he go to a physician, but that on the workman's assuring them that he did not believe the injury was serious enough to warrant that they refrained from insisting that he do so and at no time named any particular physician for him to see. Two medical witnesses, one called by the plaintiff and the other by the defendant, testified, in effect, that even if the workman had been treated by a physician from the inception of his injury, septicemia might still have developed. The court affirmed the award of the commission and the defendant appealed to the St. Louis court of appeals.

It cannot be said as a matter of law, said the court, that under the facts of this case the workman unreasonably refused to submit to medical treatment. It does not conclusively appear that he refused at all. While the defendant's witnesses testified that the workman refused to go to a physician, though repeatedly told to do so, they further testified that they merely suggested that he go to a physician or advised that he ought to do so. A mere negligent failure on the part of the workman to obtain or accept medical treatment, though advised or urged to do so, does not bar a recovery of compensation. To bar a recovery, an unreasonable refusal to submit to medical treatment must be shown and the burden of proving that refusal is on the employer. The court held that the commission was warranted in holding that the employer had failed to offer the required proof. The award of compensation was accordingly affirmed.—*Haill v. Champion Shoe Machinery Co. (Mo.), 71 S. W. (2d) 146.*

Malpractice: Negligent Treatment of Fracture.—The plaintiff sustained a simple comminuted fracture of the middle third of his right femur. The defendant-physician, apparently without attempting to reduce the fracture by nonoperative procedures, made a 10 inch incision on the right thigh and attempted to place the broken ends of the bone in juxtaposition. Thereafter infection developed and it became necessary to amputate the leg just below the hip. The plaintiff sued the defendant for malpractice and obtained judgment in the trial court, from which the defendant appealed to the Supreme Court of Appeals of West Virginia.

The plaintiff contended that it was the duty of the defendant to follow a method of treatment established and approved by physicians and surgeons generally in the same community, or similar communities, and that the defendant did not do so. In *Browning* v. *Hoffman*, 86 W. Va. 468, 103 S. E. 484, it was held, said the court, that if there are two or more approved methods of treatment of an injury a surgeon may adopt the one which, in his honest opinion, will be more efficacious and appropriate under all the circumstances, and in such case he is not liable for any injury resulting from an error in his judgment, if there is one. He is not bound at his peril to adopt the best method. In the present case the experts generally agreed that the injury could have been properly treated by the "closed" or nonoperative method. The trial court instructed the jury that it was the duty of a physician to adopt in the treatment of a case the method established and approved by physicians and surgeons generally in the community in which he performs the operation or gives the treatment and that, if they believed from the evidence that the defendant did not adopt an approved and established method of treatment of a fractured leg such as the plaintiff was suffering from at the time the treatment was administered, or if they believed from the evidence that the defendant was negligent or careless in the application of the treatment of the injury and did not use the degree of care employed by physicians and surgeons generally in the treatment as was used in the community in which he performed the operation or treatment at the time thereof, then their verdict should be for the plaintiff. This instruction, said the Supreme Court, correctly stated the law.

The fact that it became necessary, continued the court, to amputate the patient's leg did not of itself establish negligence, but it was a circumstance which the jury had the right to take into consideration in determining whether the defendant was guilty of negligence. Furthermore, according to the evidence, a roentgenogram should have been taken immediately following the operation to ascertain whether the bone was in place and without angulation. This was not done. According to the plaintiff's testimony, the defendant had neglected him for as much as five days at one time and eight days at another, during all of which time the plaintiff was undergoing much agony. While the defendant denied such neglect, the plaintiff was corroborated by another patient located in close proximity to him, and by one of the nurses. After reviewing the entire record, the Supreme Court was of the opinion that the defendant received a fair and impartial trial and that the record disclosed no reversible error. The judgment of the trial court, therefore, was affirmed.—*Maxwell v. Howell (W. Va.), 174 S. E. 553.*

Society Proceedings

COMING MEETINGS

American Orthopsychiatric Association, New York, Feb. 21-23. Miss Mary A. Clarke, 50 West 50th Street, New York, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Feb. 18-19. Dr. William D. Cutter, 535 North Dearborn Street, Chicago, Secretary.

Pacific Coast Surgical Association, Santa Barbara, Calif., Feb. 21-23. Dr. Edgar L. Gilcreest, 384 Post Street, San Francisco, Secretary.

Southeastern Surgical Congress, Jacksonville, Fla., March 11-13. Dr. Benjamin T. Beasley, 478 Peachtree Street, N.E., Atlanta, Ga., Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to Fellows of the Association and to individual subscribers to THE JOURNAL in continental United States and Canada for a period of three days. Periodicals are available from 1925 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 12 cents if two periodicals are requested). Periodicals published by the American Medical Association are not available for lending but may be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Anatomy, Philadelphia

55: 343-528 (Nov. 15) 1934

Some Features of Cleavage in Living Egg of the Rat. Elizabeth MacDonald and J. A. Long, San Francisco.—p. 343.
Anterior Hypophysis of Rabbit During Estrus and Pseudopregnancy. J. M. Wolfe, Doris Phelps and R. Cleveland, Nashville, Tenn.—p. 363.
New Formation of Arteriovenous Anastomoses in Rabbit's Ear. E. R. Clark and Eleanor Linton Clark, Philadelphia.—p. 407.
Genesis of Fossa of Allen and Associated Structures. A. W. Meyer, San Francisco.—p. 469.
Incidence of Patent Foramen Ovale Cordis in Adult American Whites and American Negroes. G. A. Seib, St. Louis.—p. 511.

American Journal of Public Health, New York

24: 1197-1284 (Dec.) 1934

Previous History of Poliomyelitis in California. J. D. Dunshee and I. M. Stevens, San Francisco.—p. 1197.
Poliomyelitis, 1934. J. L. Pomeroy and G. H. Roth, Los Angeles.—p. 1201.
Epidemiology of Poliomyelitis in California, 1934. J. P. Leake, E. T. Cedar, W. P. Dearing and A. G. Gilliam, Washington, D. C., and H. D. Chope, San Francisco.—p. 1204.
The 1934 Epidemic of Poliomyelitis in Los Angeles: Preliminary Report on Pathologic Changes in the Nervous System. R. Van Wart, C. Courville and E. M. Hall, Los Angeles.—p. 1207.
Clinical Features of Poliomyelitis in Los Angeles. A. G. Bower, R. W. Meals, Mary Bigler, J. Ewing and V. Hauser, Los Angeles.—p. 1210.
The 1934 Epidemic of Poliomyelitis in Southern California. G. M. Stevens, Los Angeles.—p. 1213.
*Use of Serum and Routine and Experimental Laboratory Findings in the 1934 Poliomyelitis Epidemic. J. F. Kessel, A. S. Hoyt and R. T. Fisk, Los Angeles.—p. 1215.
Orthopedic Aspect of the Los Angeles County 1934 Poliomyelitis Epidemic. T. M. Hart and J. V. Luck, Los Angeles.—p. 1224.
Poliomyelitis in San Francisco. E. B. Shaw and H. E. Thelander, San Francisco.—p. 1229.
Western Public Health Problems. J. L. Pomeroy, Los Angeles.—p. 1234.
Secondary Cases of Certain Communicable Diseases Among Nonimmune Family Contacts. F. L. Kelly and Eleanor Reite, Berkeley, Calif.—p. 1240.
Silicosis: Study of One Hundred and Six Pottery Workers. P. A. Quaintance, Los Angeles.—p. 1244.
Salmon Inspection. R. W. Clough and E. D. Clark, Seattle.—p. 1252.

The Los Angeles Poliomyelitis Epidemic.—Kessel and his associates state that the mortality rate of the 1934 poliomyelitis epidemic in Los Angeles has been exceptionally low and the amount of residual paralysis less than usual. The proportion of adults infected has been higher than is common. An exceptionally high rate of communicability has been noted. This was especially apparent among hospital employees in the communicable disease unit of the Los Angeles County Hospital, of whom 11.9 per cent developed poliomyelitis. Certain preliminary observations from the laboratory during this epidemic are as follows: Employees receiving convalescent pooled and normal pooled poliomyelitis serum as a prophylactic measure demonstrated no less degree of susceptibility than employees working under similar conditions who received no serum. There is slight evidence that those receiving prophylactic serum developed less severe symptoms than those who received no serum. Convalescent pooled serum was no more effective when given therapeutically than normal pooled serum. A small proportion of the patients reported serum reactions, ranging from a mild to a severe type of serum sickness. A high proportion of those who demonstrated positive serum symptoms responded to skin sensitivity tests with human serum. Spinal cell counts of poliomyelitis cases demonstrated that 27 per cent showed no white cells, 38 per cent from 1 to 9 cells, and 35 per cent 10 or more cells. Of those showing more than 10 cells, 50 per cent gave a positive colloidal benzoin reaction. Attempts to inoculate monkeys with virus from eleven necropsy cases have given positive results in five. The virus appears to possess an antigenic relationship to the M. V. strain, since monkeys that recovered from inoculation with the California strain are resistant to subsequent inoculation with the M. V. strain.

American Journal of Surgery, New York

26: 415-612 (Dec.) 1934

Studies on Thyroid Disorders: VII. Correct and Incorrect Use of Iodine in Treatment of Goiter. E. Goetsch, Brooklyn.—p. 417.
Upper Urinary Tract During Normal Pregnancy. J. S. Lewis Jr. and E. C. Baker, Youngstown, Ohio.—p. 431.
*Danger of Sudden Deflation of Acutely Distended Bowel in Late Low Intestinal Obstruction. R. Elman, St. Louis.—p. 438.
*Gastric Acidity in Carcinoma of Stomach. M. W. Comfort, Rochester, Minn., and Frances R. Vanzant, Minneapolis.—p. 447.
The Iodoiodikon Liver Function Test as an Index of Postoperative Morbidity in Cholecystectomy. C. W. Cutler, Jr., New York.—p. 457.
Unusual Complication with a Levine Tube. P. W. Greeley, Winnetka, Ill.—p. 466.
Subphrenic (Subdiaphragmatic) Abscess. L. M. Bogart, Flint, Mich.—p. 467.
Infusion Reactions, with Especial Reference to "Speed Shock." A. H. Milbert, New York.—p. 479.
Bacterial Invasion of Blood Stream. R. Ottenberg, New York.—p. 486.
Surgical Conditions of Knee Joint. M. S. Henderson, Rochester, Minn.—p. 499.
*Air Cushion Reduction of Incomplete Vertebral Fracture Dislocations, Associated with Spinal Cord Injuries. B. Stookey, New York.—p. 513.
Evipal Sodium: Short Intravenous Anesthesia. E. M. Livingston, S. Emy and H. Lieber, New York.—p. 516.
Clinical Results from Use of New and Superior Antiseptic Solution. W. L. Secor, Kerrville-on-the-Guadalupe, Texas.—p. 522.
Ideals in Rhinoplastic Surgery. W. W. Carter, New York.—p. 524.
Grafts and Transplants. F. Beekman, New York.—p. 528.

Danger of Sudden Deflation of Acutely Distended Intestine.—Elman made a few clinical and experimental observations which suggest that serious symptoms and death may be caused by sudden decrease of the high intra-intestinal pressure present in the distended intestine in certain late cases of low intestinal obstruction. That the unfavorable result is directly connected with the coincident release of the intra-intestinal pressure seems to be suggested from the evidence. The lethal outcome that may occur after surgical deflation of a tense obstructed intestine must be due either to the operation itself (anesthesia, surgical shock) or to some untoward result of the procedure employed during the operation. The idea of Wilkie's that death is a circulatory one due to extensive loss of blood and fluid into the paralyzed dilated splanchnic capillaries is not supported by the clinical symptoms of these patients or by their failure to respond even when large amounts of blood and fluid are given. If one assumes that the fall of intra-intestinal pressure may actually be the cause of death, it is easy to explain the train of events on a mechanical basis. In a distended obstructed intestine, circulatory changes in the wall begin soon and in a few days may become quite marked and in fact lead to localized patches of gangrene showing through and often involving the muscularis of the wall opposite the mesentery where the circulation is the poorest. Even in the absence of visible gangrene there is ample evidence of edema, swelling and foci of necrosis and even actual loss of the mucosa in fatal cases examined at necropsy. The normal intestinal mucosa is a rather efficient barrier against the entrance of the many poisonous fecal elements that swarm in abundance in perfectly normal contents of the lower intestine. This barrier depends on the selective action of living intestinal epithelium. When these epithelial cells become damaged this power must be impaired, and poisons and bacteria may traverse the barrier from the intestinal lumen into the circulation. It is not the mere presence of damaged mucosa that is important. Postoperative toxemia is probably due to the fact that, while intra-intestinal pressure is high enough to interfere with the blood flow through the intestinal wall, an efficient barrier is still present between the fecal content and the circulation; provided, that is, that the pressure is not great enough to force passage through the entire intestinal wall into the peritoneal cavity. According to this idea, then, the intestinal distention for a time at least acts as a protection against absorption of toxins or bacteria. Now, whenever the intra-intestinal pressure falls

sufficiently, the blood flow through the intestinal wall begins again and there is nothing now to prevent intestinal toxins and bacteria from entering the dilated capillaries. The failure to demonstrate toxins or bacteria in the blood of patients or animals sick or dying of low intestinal obstruction does not necessarily invalidate the theory. This conception fits in with the unpredictable behavior of these cases clinically and experimentally. The element of intra-intestinal pressure in preventing or promoting a toxemia in late low intestinal obstruction by its effect on the barriers is one that merits greater study and consideration.

Gastric Acidity in Carcinoma of Stomach.—Comfort and Vanzant studied the records of 619 men and 186 women with carcinoma of the stomach, in whom the nature of the disease was confirmed at operation or by subsequent observation and the results of gastric analysis were available. In cases of carcinoma of the stomach, the incidence of achlorhydria was about three times the normal and the mean free acidity was lowered about 14 points in men and 8 in women. Curiously, carcinoma seems to injure the acid-secreting mechanism of men more than it injures that of women. The range of acidity for men with carcinoma of the stomach was found to be from 0 to 90 units, which is only 10 points short of the range for normal men. On comparing percentage distribution curves of acidity of normal persons and of patients with carcinoma of the stomach, it was seen that the difference comes in the upper part of the range beyond the point marking 20 units. In the group of patients with carcinoma of the stomach who had free acid, the total acidity was but slightly lower than normal. In this group the combined free acidity was slightly above normal. In the achlorhydric group, the total acidity was slightly above normal. The incidence of achlorhydria increased with age among persons with carcinoma of the stomach just as it does among normal persons. The only difference was that the actual percentages at the different ages were greater. Among men with carcinoma of the stomach there was the normal falling off in free acidity with age, but the curve was different from that of normal men. Gastric acidity was not influenced markedly by the degree of anemia, loss of weight, situation of the growth or the volume of gastric contents. Marked differences in gastric acidity were noted when the cases of carcinoma of the stomach were divided into three groups, according as they had either an ulcer-like, a pseudo-ulcer or a nonulcer type of history. In the ulcer-like group the incidence of achlorhydria and the range of free acidity were practically normal and mean free acidity was only 5 or 10 units below normal. The two distribution curves were almost identical. In the nonulcer group the incidence of achlorhydria was about four times normal. The range of free acidity was shortened by about 40 units, and mean free acidity was lowered by 20 units in the case of men and by 10 units in the case of women. In the pseudo-ulcer group, the distribution curve representing acidity lay between the other two curves but somewhat nearer that of the group in which the history was not that of ulcer. The data suggest that in the nonulcer group the carcinoma often develops in an anacid stomach, and that in the ulcer-like group the lesion begins in a normally acid stomach.

Method for Reduction of Vertebral Fracture Dislocations.—Stookey presents a method for the reduction of incomplete fracture dislocations that may be employed immediately after the injury, can be maintained as long as may be desired, and is available in any hospital having an air mattress. Reduction of the dislocation is accomplished without manipulation and usually no special skill is required. With slight modifications the principle of the method may be used for transporting patients with acute spinal cord injuries by substituting a stretcher for the bed and using an air mattress. The technic used is as follows: A fracture board is placed on the springs in the usual manner. The foot end of the bed is placed on low blocks elevated slightly in order to raise the relative position of the patient's head to his trunk. In order to have the head easily accessible, the foot end of the bed is made the head of the bed. Two ordinary mattresses are placed over the fracture board. A blanket is then rolled and placed on the ordinary mattresses at the level of the shoulders for fracture dislocations of the cervical vertebrae or at whatever level may be indicated for fractures of other regions of the spine. An air mattress, preferably 8 inches thick, is then placed on the bed over the blanket roll and a strip of adhesive tape, 8 inches wide if the fracture is in the cervical region or from 12 to 14 inches wide if the fracture is in the thoracic or the lumbar region, is applied to the mattress beginning at the line of the blanket roll. The mattress is covered with a soft woolen blanket or a sheet and the patient is placed on the bed. The adhesive strip is then drawn as tight as possible, as much force being used as is necessary to obtain the proper degree of angulation of the air mattress. It is then fastened to the bottom of the foot piece of the bed either directly or to a movable bar attached to the foot end, a ratchet being used to tighten as needed. The air mattress must not leak and must be kept pumped up, and the adhesive strip must be tight at all times. A pillow is then rolled and placed beneath the patient's knees so as to flex the lower extremities slightly. A small folded blanket is placed beneath the calf muscles, reaching to within 4 inches of the insertion of the achilles tendon. The heels are thus kept off the bed by resting the calves on a wide surface and pressure sores of the heels are thus avoided. Any abnormal position of this sort is naturally uncomfortable and the author has found it advisable to relieve the patient's discomfort during the first few days by medication. If each of the details is carefully observed, he believes that the foregoing method will be found satisfactory for the reduction of incomplete vertebral fracture dislocations, especially in the cervical region, and for the reduction of compression fractures of the whole spine.

Archives of Dermatology and Syphilology, Chicago

30: 761-916 (Dec.) 1934

The Roentgen Unit in Dermatology. G. M. MacKee and A. C. Cipollaro, New York.—p. 761.
Lupus Erythematosus Disseminatus Acutus Haemorrhagicus. W. T. Garfield, C. W. Steele and J. D. Houghton, Boston.—p. 772.
*Origin and Nature of Pigmented Nevi (Schwannomas). S. W. Becker, Chicago.—p. 779.
Granuloma Annulare: Report of Unusual Case. F. H. Grauer, Ann Arbor, Mich.—p. 785.
Lichen Nitidus: Report of Generalized Case. M. S. Wien and Minnie Oboler Perlstein, Chicago.—p. 790.
Superficial Intra-Oral Application of Roentgen Rays. L. Hollander and A. Fisher, Pittsburgh.—p. 793.
*Necrobiosis Lipoidica Diabeticorum. E. P. Zeisler and M. R. Caro, Chicago.—p. 796.
*Hinton Test and Lumbar Puncture in Treated Primary and Secondary Syphilis. W. A. Hinton, Boston.—p. 813.
*Common Warts: Effective Treatment. H. Sutherland-Campbell, Los Angeles.—p. 821.
Lymphogranuloma Inguinale: I. Preservation of Frei Antigen by Drying: Its Concentration in Fresh and in Dried Pus. A. W. Grace, with technical assistance of Florence H. Suskind, New York.—p. 823.
Esthiomene, Late Manifestation of Lymphopathia Venerea (Lymphogranulomatosis Inguinalis). M. Dorne and S. J. Zakon, Chicago.—p. 831.
*Postencephalitic Trophic Ulcer. S. S. Greenbaum and B. J. Alpers, Philadelphia.—p. 837.
Dermatomycosis and the Soldier. D. J. Wilson, Omaha.—p. 841.
Use of Nitrites for Relief of Pruritus. M. Prinzmetal, Boston.—p. 843.
High Pathogenicity of Recently Isolated Strain of Spirochaeta Pallida. C. K. Hu, New York.—p. 847.

Origin and Nature of Pigmented Nevi.—Becker states that the examination of several hundred pigmented nevi by modern histologic methods showed that they consisted of one or two types or a combination of the two. The first is the strictly cellular type, which results from the multiplication of the clear cells in the epidermis, with or without penetration into the dermis; the second is the nerve type, which is deeper and the structures of which often simulate those of tactile corpuscles. The use of the term "schwannoma," as suggested by Masson, is not illogical, although more work must be done before the origin of clear cells and nevi in the sheath of Schwann can be proved. The terms nevus and nevoid are ambiguous and could be replaced by the term prenatal without losing any of their significance.

Lipoid Diabetic Necrobiosis.—Zeisler and Caro report two cases of lipoid diabetic necrobiosis (Urbach-Oppenheim), with postmortem observations in one case. Lipoid diabetic necrobiosis is a rare disease of the lipoid and carbohydrate metabolism, characterized by yellow to buff-colored scleroderma-like plaques on the lower extremities. The histologic changes

are pathognomonic and consist primarily of vascularitis with perivascular lymphocytic infiltration and extensive necrobiotic areas in the corium containing swollen collagen fibers, which are infiltrated by droplets of lipoids of undetermined nature. The pathogenesis of the disease is explained by a deposition or imbibition in the necrobiotic intercellular connective tissue of the excess lipoids present in the blood, following changes in the cutaneous blood vessels caused by the diabetes. The lesions must be differentiated from xanthoma, amyloidosis, scleroderma and similar dermatoses. The disease is chronic and is resistant to treatment with insulin and to diets low in fat.

Hinton Test and Lumbar Puncture in Syphilis.—Hinton made a study of 361 consecutive patients with primary and secondary syphilis to ascertain what effect the use of the Hinton blood test would have on the number of examinations of spinal fluid that are desirable as aids in determining the persistence of the infection within the first two years of the disease. In each case the diagnosis of syphilis was made on a combination of definite clinical and laboratory criteria. Seventy per cent of the cases of primary syphilis gave positive results in a dark field examination, and all cases of secondary syphilis showed a positive reaction of the blood with a rash or other unmistakable signs of the secondary stage. Of the 361 patients, 153 were under observation and treatment for more than twelve months and had blood tests between the twelfth and eighteenth months. Of the remaining 208 patients, sixteen in the primary stage never had a positive reaction of the blood or later clinical signs of the disease; 182 patients were under observation or treatment for less than a year, and ten of those observed and treated for more than twelve months had no blood tests between the twelfth and eighteenth months. The observations of the 153 cases have pointed out that, with the aid of an unusually sensitive blood test for syphilis, lumbar punctures are not necessary during the first two years of the disease for the purpose of determining the persistence of the infection. That the infection may persist, in spite of even a negative reaction to the Hinton test, has been indicated by serologic relapses in twelve cases. In none of six of these cases in which lumbar puncture was done did the examination of the spinal fluid help more than the Hinton test in determining this persistence.

Treatment for Common Warts.—Sutherland-Campbell first used the following procedure on a patient who was given a maximum of roentgen and radium therapy for warts that involved the finger-tips of both hands, without effect. With a fine spark, the verrucous surfaces were seared lightly. The patient returned at weekly intervals, and the procedure was repeated. Involution and desquamation of the lesions occurred within six weeks. At this time the author attributed the reaction to (1) a result of the combined action of the treatment with rays of short wavelength and the superficial electrodesiccation or (2) spontaneous healing. Use of the procedure for twelve months has demonstrated to him that it is the method of choice and is the solution of what can be a vexing problem. The degree of pain experienced during treatment, except in rare instances, is negligible and tolerated easily. In only one case has it been necessary for the author to use procaine hydrochloride. The method is superior to surgical removal or electrodesiccation proper. The method may be termed superficial fractional desiccation. In employing it the surface of the wart is cleansed. A moderate spark is used commencing inside the margin of the corneus collaret, the border of the wart is circled, and then only the surface of the wart proper is seared and carbonized. The procedure is repeated at biweekly intervals. There have been no recurrences following five or six treatments, which is the number given ordinarily. Only one patient with plantar warts has been subjected to this form of therapy, with the usual good result.

Postencephalitic Trophic Ulcer.—Greenbaum and Alpers believe their case to be the first reported instance in America of trophic ulceration of the skin occurring during the chronic stages of epidemic encephalitis. Although the condition is benign, it is diagnostically important. It is generally believed that trophic ulcers are the result of two factors: trauma, usually in the form of pressure, and degenerative changes in the sensory and nutrient fibrillae of the affected nerves. The latter factor is, of course, essential and occurs in connection with a number of diseases of the central and peripheral nervous system, but trauma (mechanical or infectious, or both) is of undoubted etiologic importance. All the ulcers reported in the German literature occurred in practically the same location: the nasolabial groove. Itching at the site of the ulcer was a usual premonitory and accompanying symptom. The first case was reported by Hoffmann in 1926. In the same year Lammerman reported a case, in 1929 Petzal reported the third, and in the same year Schlitter reported the fourth case.

Archives of Otolaryngology, Chicago

20: 765-884 (Dec.) 1934

Agranulocytosis (Malignant Neutropenia). R. F. Ridpath, Philadelphia.—p. 765.
Further Research on Experimental and Clinical Sinusitis. O. Larsell and R. A. Fenton, Portland, Ore.—p. 782.
*Prenatal Medication as Possible Etiologic Factor of Deafness in the New-Born. H. M. Taylor, Jacksonville, Fla.—p. 790.
Incidence of Allergy in Rhinologic Practice. H. L. Baum, Denver.—p. 804.
*Sinus Headache: Differentiated from Headaches of Other Origin. C. C. Fox, Philadelphia.—p. 813.
Immunization of Upper Respiratory Tract. T. E. Walsh and P. R. Cannon, Chicago.—p. 820.
Peritonsillar Spaces: Anatomic Study. G. B. Wood, Philadelphia.—p. 837.
Roentgenologic Examination of Maxillary Sinus Before and After Operation. E. King, Cincinnati.—p. 842.
Sequels of Scarlet Fever Involving Temporal Bones, Paranasal Sinuses, Meninges and Lateral and Cavernous Sinuses, with New Bone Formation in Jugular Bulb. A. J. Cone and D. Wolff, St. Louis.—p. 849.
Transphenoidal Injection of Iodized Poppy Seed Oil into Hypophyseal Cyst: Report of Case. F. H. Linthicum, Los Angeles.—p. 861.

Prenatal Medication as the Possible Etiology of Deafness.—Taylor suggests that perhaps the reason why the otologist has practically ignored the subject of prenatal medication as a possible etiologic factor of deafness in the newborn is that a child must be 2½ or 3 years old before a diagnosis of nerve deafness can be made. By that time the prenatal history has been dismissed. The history which the otologist usually endeavors to get consists principally of whether there has been a family history of deafness, consanguinity, hereditary syphilis or meningitis, and with these details the subject is generally closed. To some, however, the history of the drugs given the mother during pregnancy is of as much importance as whether the patient had a great-uncle or a second cousin who was deaf. If it were possible to ascertain the incidence of nerve deafness among the children registered in schools for the deaf in the United States, and, by questioning the mothers, to gather information regarding their intake during pregnancy of drugs which may produce nerve deafness, the results might constitute a dramatic incident in the history of otology. The author states that certain drugs have a predilection for the auditory nerve. Idiosyncrasy for drugs may be an important factor in causing nerve deafness. Quinine takes precedence among the drugs causing nerve deafness and is frequently used during the term of pregnancy. Evidence has been presented that certain drugs which have a predilection for the auditory nerve readily pass through the placenta when administered to the pregnant mother and may be toxic to the fetus, a possibility which the otologist has virtually ignored. Prenatal medication as a possible etiologic factor of deafness in the new-born is of sufficient importance to warrant the cooperative research of the biochemist, the histopathologist, the obstetrician and the otologist.

Sinus Headache.—Fox says that in acute sinusitis there are two general types of pain: the neuralgic and a constant type, more or less localized in the region of the diseased sinus. The neuralgic type of pain is invariably present during the morning and gradually disappears before early afternoon. This pain may be followed by a sensation of fulness and pressure in the sinus. The pain begins in the sinus but may be so severe as to involve adjacent nerves. The second type of pain in acute cases is constant discomfort in the region of the sinus. It is due to involvement of the mucous membrane or bony wall of the sinus. There is usually marked stagnation of secretions, and the sinus is sensitive to palpation. The pain may be a dull ache or soreness, becoming at times more intense.

In chronic sinusitis the headache is more diffuse and often indefinite. Early acute maxillary sinusitis usually causes the sensation of pressure, fulness and distention in the sinus. The pain may be a dull ache or may be neuralgic. In chronic maxillary sinusitis the patient may have no pain to warn him of infection. In fact, pain is often not present in chronic cases. In acute frontal sinusitis, headache is the most constant symptom. Acute ethmoid sinusitis can cause pain that is difficult to distinguish from that due to frontal sinusitis. The pain may be a dull pressure or an intense headache. Involvement of the anterior cells causes dull pain between the eyes at the root of the nose. Burning in the eyes, lacrimation and increase of pain when the eyes are used for long periods are typical. The pain is steady, without severe exacerbations. When the posterior ethmoid cells are involved there is temporal, occipital or parietal headache, which is increased by using the eyes. Pain is most often present along the first, and at times the maxillary, division of the nerve, causing pain in the face, which may be confused with that of an antral lesion or tic douloureux. In acute sphenoid sinusitis the pain may be an intense sensation of pressure deep in the head, in the posterior half of the head or behind the eyeball, over the vertex, just behind the mastoid process and even in the middle ear. The pain in chronic sphenoid sinusitis is unreliable. Most often it is a feeling of pressure and fulness deep in the head and occipital region, with sometimes stiffness of the neck. Pain in the vertex or temple is frequently present.

Arch. of Physical Therapy, X-Ray, Radium, Chicago

15: 709-764 (Dec.) 1934

Fortification of Milk with Vitamin D. J. H. Shrader, Baltimore.—p. 709.

Physical Therapy from the Standpoint of the Internist. T. P. Sprunt, Baltimore.—p. 719.

Physical Therapy in Preventive Medicine. F. T. Woodbury, Poughkeepsie, N. Y.—p. 723.

Treatment of General Paresis by Electropyrexia. R. H. Kuhns, Elgin, Ill.—p. 725.

Value of Electrocardiograph in Cardiac Disease. L. E. Cooley, Dubuque, Iowa.—p. 729.

Treatment of Hemiplegia. A. A. Martucci, S. B. Hadden and B. McGlone, Philadelphia.—p. 734.

Colorado Medicine, Denver

31: 425-468 (Dec.) 1934

Acute Conditions Simulating Surgical Abdomen. W. H. Mast, Gunnison.—p. 428.

Rôle of Ophthalmoscope in General Practice. R. W. Danielson, Denver.—p. 433.

Delaware State Medical Journal, Wilmington

6: 247-266 (Nov.) 1934

Acquired External Fecal Fistulas Involving Anterior or Lateral Abdominal Wall. A. P. Heinick, Chicago.—p. 247.

Acute Coronary Thrombosis. O. S. Allen, Wilmington.—p. 252.

Diagnostic Pointers in Cardiology. E. Podolsky, Brooklyn.—p. 258.

Florida Medical Association Journal, Jacksonville

21: 179-224 (Nov.) 1934

Surgical Treatment of Pulmonary Tuberculosis. K. A. Morris, Jacksonville.—p. 189.

Intestinal Obstruction, Statistical Study. J. S. Stewart Jr., Miami.—p. 194.

The Mentally Ill Citizen: His Care, Especially as Applied to Florida. Beverley R. Tucker, Richmond, Va.—p. 197.

Iowa State Medical Society Journal, Des Moines

24: 603-654 (Dec.) 1934

Some Causes of Professional Unrest. R. G. Leland, Chicago.—p. 603.

Value of Resection of Presacral Nerve. W. D. Abbott, Des Moines.—p. 607.

Borderline Psychoses: Problem in Differential Diagnosis. W. Malamud, Iowa City.—p. 610.

Significance of Urinary Findings in Nephritis. F. P. McNamara, Dubuque.—p. 614.

Promotion of Immunization by the State Department of Health. J. H. Kinnaman, Des Moines.—p. 618.

Radiation Treatment of Small Fibroids and Menorrhagias. B. T. Whitaker, Boone.—p. 620.

Insulin. J. C. Shrader, Fort Dodge.—p. 622.

Peptic Ulcer. E. G. Senty, Davenport.—p. 624.

Significance of Systolic Apical Murmurs. E. L. Wurtzer, Clear Lake.—p. 626.

Human Anthrax: Case. A. H. Quin Jr., Des Moines.—p. 627.

Johns Hopkins Hospital Bulletin, Baltimore

55: 295-360 (Nov.) 1934

Studies on Physiology of Parathyroid Glands: VII. Some Responses of Normal Human Kidneys and Blood to Intravenous Parathyroid Extract. R. Ellsworth and J. E. Howard, Baltimore.—p. 296.

Calcium and Phosphorus Studies: X. Effect of Variation of Calcium, Phosphorus and of Vitamin D in Diet on Iron Retention in Rats. D. H. Shelling and H. W. Josephs, Baltimore.—p. 309.

Id.: XI. Effect of Prophylactic and Curative Doses of Standardized Viosterol on Human Tissues: Necropsy Report on Thirteen Cases Showing No Tissue Damage. D. H. Shelling and Deborah A. Jackson, Baltimore.—p. 314.

Mechanism of Anemia in Infancy: Physiologic Anemia. H. W. Josephs, Baltimore.—p. 335.

Lead Poisoning: Report of Case in Child with Extensive Peripheral Neuritis. T. C. Goodwin, Baltimore.—p. 347.

Journal of Bacteriology, Baltimore

28: 433-540 (Nov.) 1934

Enzymes of Bacteria and Bacterial Metabolism. A. I. Virtanen, Helsinki, Finland.—p. 447.

Present Status of Problem of Sugar Fermentation. C. Neuberg and Maria Kobel, Berlin-Dahlem, Germany.—p. 461.

Some Physiologic Characteristics of Propionic Acid Bacteria. E. R. Hitchner, Madison, Wis.—p. 473.

Capsules in Young Cultures of Streptococcus Haemolyticus. C. V. Seastone, Boston.—p. 481.

Bacteriologic Changes in Acidophilus Milk at Room and Icebox Temperatures. Lenore M. Kopeloff, J. L. Etchells and N. Kopeloff, New York.—p. 489.

Lactobacillus Bifidus. J. E. Weiss and L. F. Rettger, New Haven, Conn.—p. 501.

Pleo-Antigenicity of a Variant of Proteus X19. H. Welch, Hartford, Conn., and A. K. Poole, New Haven, Conn.—p. 523.

Journal of Experimental Medicine, New York

60: 661-806 (Dec. 1) 1934

Hemorrhages in Skin Lesions of Guinea-Pigs Following Intravascular Injection of Toxins (Shwartzman Phenomenon). J. Freund, New York.—p. 661.

Hemorrhages in Tuberculous Guinea-Pigs at Site of Injection of Irritants Following Intravascular Injections of Injurious Substances (Shwartzman Phenomenon). J. Freund, New York.—p. 669.

Comparison of Hematocytologic Constitution of Male and Female Rabbits. P. D. Rosahn, Louise Pearce and C.-K. Hu, New York.—p. 687.

Virus Induced Mammalian Growth with Characters of Tumor (the Shope Rabbit Papilloma): I. Growth on Implantation Within Favorable Hosts. P. Rous and J. W. Beard, New York.—p. 701.

Id.: II. Experimental Alterations of Growth on Skin: Morphologic Considerations: Phenomena of Retrogression. J. W. Beard and P. Rous, New York.—p. 723.

Id.: III. Further Characters of Growth: General Discussion. P. Rous and J. W. Beard, New York.—p. 741.

Ultrafiltration of Virus of Poliomyelitis. M. Theiler and J. H. Bauer, New York.—p. 767.

Problem of Significance of Inclusion Bodies Found in Salivary Glands of Infants, and Occurrence of Inclusion Bodies in Submaxillary Glands of Hamsters, White Mice and Wild Rats (Peiping). Ann G. Kuttner and S.-H. Wang, Peiping, China.—p. 773.

Journal of Immunology, Baltimore

27: 515-590 (Dec.) 1934

Absorption of Tetanus Toxin by Brain Tissue of Animals of Various Ages. Agnes R. Beebe, New Haven, Conn.—p. 515.

*Fatal Pseudo-Anaphylaxis by Intramuscular Injection of Benzene and Related Substances. P. E. Steiner, Chicago.—p. 525.

Experimental Studies of Puerperal Infection: IV. Effect of Pregnancy on Hemolytic and Agglutinative Activity of Blood Serum. C. C. Torrance, Albany, N. Y.—p. 531.

Immunization Against Typhoid Fever with Heterobacterigen. C. Suzuki and K. Sugio, Formosa, Japan.—p. 539.

Comparison of Agglutinogens in Rabbits with Those in Man. W. C. Boyd and D. Feldman, Boston.—p. 547.

Formaldehyde and Serum Proteins: Their Immunologic Characteristics. F. L. Horsfall Jr., Boston.—p. 553.

Formaldehyde Hypersensitiveness: Experimental Study. F. L. Horsfall Jr., Boston.—p. 569.

Pseudo-Anaphylaxis Following Injection of Benzene.—Steiner produced fatal pseudo-anaphylactic shock in guinea-pigs and other species by repeated intramuscular injection of benzene and related chemicals. Death was due to bronchospasm. Similar reactions were caused by the inhalation and the intravenous injection of benzene in animals who had had no previous experience with the drug. The spasm was not relieved by epinephrine or atropine. It appeared quickly and disappeared with equal rapidity after forced ventilation of the lungs. Repeated intramuscular injections were necessary, not to cause a state of true allergy, but to produce an area of inflammation from which the benzene at subsequent injections

was absorbed in sufficient amounts to produce a bronchospasm. The author suggests that the bronchospastic action of benzene shown in these experiments on animals possibly applies to human bronchi and offers an alternative explanation for these acute deaths in man. In view of these results the use of intramuscular benzene injections in the treatment of bronchial asthma, as reported recently by Kairiukstis, should proceed with caution.

Journal of Lab. and Clinical Medicine, St. Louis

20: 227-336 (Dec.) 1934

Effects of Hyperpyrexia Induced by Physical Means on Complement Fixing Antibodies. L. G. Hadjopoulos and W. Bierman, New York.—p. 227.
*Mercuric Chloride Poisoning Treated by Exsanguination-Transfusion: Case. E. H. Hashinger and J. F. Simon, Lawrence, Kan.—p. 231.
Nodular Granulomatous Lesions of Liver, Spleen and Lymph Nodes: Probably an Atypical Form of Hodgkin's Disease. D. C. Beaver and A. M. Snell, Rochester, Minn.—p. 236.
Allergic Phases of Arthritis. G. T. Brown, Washington, D. C.—p. 247.
Phosphatase in Heterotopic Bone Formation Following Transplantation of Bladder Mucosa. E. M. Regen and W. E. Wilkins, Nashville, Tenn.—p. 250.
Menstrual Influence on Blood Morphology: Note. A. W. Rowe and Mary C. Guagenty, Boston.—p. 253.
*Factors Influencing Sedimentation Rate of Erythrocytes. T. H. Cherry, New York.—p. 257.
Lipase and Esterase in Blood Serum: Their Diagnostic Value in Pancreatic Disease. M. W. Comfort and A. E. Osterberg, Rochester, Minn.—p. 271.
Prognosis of Coronary Thrombosis Based on Nonprotein Nitrogen in Blood. C. L. Steinberg, Rochester, N. Y.—p. 279.
Modified Technic for Sternal Puncture and Its Value in Hematologic Diagnosis. C. Reich, New York.—p. 286.
Comments and Procedure on Thick Blood Film Technic. J. Benavides, Panama, Republic of Panama.—p. 289.
Biologic Diagnosis of Teratoma Testis. S. E. Owen, Hines, Ill.—p. 296.
Friend's Method for Estimation of Chlorides: Note. J. E. Hearn, New York.—p. 302.
Determination of Urine Chlorides with Mercuric Nitrate. C. E. Holdridge and J. W. Cavett, Minneapolis.—p. 303.
New Procedure for Introducing Solutions Directly in Small Intestine of Experimental Animals. S. Maddock, Boston.—p. 304.
Simplified Technic for Colorimetric Determination of Blood Cholesterol. R. S. Fidler, Columbus, Ohio.—p. 307.
Protein Analyses in Cerebrospinal Fluid: Comparative Study of Methods. B. S. Walker and H. J. Bakst, Boston.—p. 312.
Further Observations on Colloidal Carbon Flocculation Test in Spinal Fluid. P. G. Schube, Boston.—p. 314.
*Micromethod for Determination of Blood Nonprotein Nitrogen. H. Irving and J. C. Forbes, Richmond, Va.—p. 316.
New Method for Determination of Blood Cell Volume. S. J. Mason, Cincinnati.—p. 318.
Simple Apparatus for Keeping Citrated Blood Warm During Injection. L. Heddick, Whittier, Calif.—p. 321.

Mercuric Chloride Poisoning Treated by Exsanguination-Transfusion.—Hashinger and Simon report a case of mercuric chloride poisoning in which they employed exsanguination-transfusion. It was done for two reasons: First, as shown by Rosenbloom and others, the blood and other tissue juices contain the greater part of the absorbed mercury, so that replacing of the blood will remove the poison in the largest possible quantity. Second, if the blood is replaced in sufficient quantity, the nitrogenous products retained in the body will be diluted and kept at a sublethal level until the renal epithelium can regenerate. In addition to the bleeding followed by transfusions, the patient was given a small amount of sodium thiosulphate for its reported value in neutralizing available mercury. Sodium chloride was given to combat loss of chlorides by vomiting. When the patient was seen seven months after dismissal, examination showed the urine to be entirely negative. The systolic blood pressure was 140 and the diastolic 80 and chlorides 460. Clinically the patient was well.

Sedimentation Rate of Erythrocytes.—It appears to Cherry that changes in the blood sedimentation time are caused by disturbing the fine balance between the cellular and fluid elements in the circulation. Cell volume and the variations of fibrin, euglobulin and globulin in the plasma apparently influence the change of rate. These variations from normal occur in so many pathologic states, thus influencing the settling of the erythrocytes, that it is impossible to affix definitely a standard sedimentation rate to any disease. To interpret this test for diagnostic purposes, the cell volume and nitrogen partitions must be determined if it is to be of any value. The sedimentation test alone is confusing. Of two persons having the same disease, one will frequently show a sedimentation rate in the fast group and the other in the slow group. As a prognostic aid it is of slight help. A very rapid sedimentation rate does not by any means indicate a poor outlook for recovery; it indicates that toxic absorption and tissue destruction are progressing so rapidly that production of biochemical changes in the blood stream is taking place, and this causes the imbalance of the sanguineous elements. The leukocyte count or filament-nonfilament study in conjunction with the clinical picture is of much greater aid than the sedimentation rate.

Micromethod for Determination of Nonprotein Nitrogen.—The procedure that Irving and Forbes use for the determination of blood nonprotein nitrogen is essentially the same as Folin and Wu's method, except that one-fifth the amount of each solution is used and the tubes are graduated at the 10 cc. instead of the 50 cc. mark. The procedure is as follows: One cc. of blood filtrate is transferred to a Pyrex test tube, 150 by 15 mm., graduated at 10 cc.; 0.2 cc. of Folin and Wu digestion mixture is added, and digestion is carefully carried out in the usual manner. Distilled water is then added to the 10 cc. mark, the solution is mixed, and 3.5 cc. of Koch's Nessler solution is added. A standard is prepared at the same time, using 2 cc. of an ammonium sulphate solution (1 cc. = 0.02 mg. normal); 0.2 cc. of digestion mixture is added, diluted to 10 cc., and 3.5 cc. of Nessler solution is added. The finger tip method is essentially the same as the foregoing: Two-tenths cc. of blood is measured in a special pipet and added to 3.4 cc. of distilled water in a 15 cc. centrifuge tube, the pipet being rinsed out several times with the diluting fluid; then 0.2 cc. of a 10 per cent solution of sodium tungstate is added, followed by 0.2 cc. of two-thirds normal sulphuric acid. After mixing and standing for several minutes, the tube is centrifugated at a moderately high rate of speed; then 2 cc. of the supernatant fluid is carefully digested with 0.2 cc. of digestion mixture and analyzed as described. If desired, the supernatant liquid may be filtered through a small filter paper after centrifugating, but this is as a rule unnecessary.

Journal of Nutrition, Philadelphia

8: 615-754 (Dec. 10) 1934

New Toxicant Occurring Naturally in Certain Samples of Plant Foodstuffs: III. Hemoglobin Levels Observed in White Rats Which Were Fed Toxic Wheat. K. W. Franke and V. R. Potter, Brookings, S. D.—p. 615.
Id.: IV. Effect of Proteins on Yeast Fermentation. K. W. Franke and A. L. Moxon, Brookings, S. D.—p. 625.
Effect of Prunes and Water Extract of Prunes on Plasma Carbon Dioxide Combining Capacity and Composition of Urine When Included in Acid, Neutral and Uncontrolled Diets. E. Mrak, C. Smith, J. Fessler, H. Lambert and T. Harper, Berkeley, Calif.—p. 633.
Human Milk Studies: XVI. Vitamin D Potency as Influenced by Supplementing Diet of Mother During Pregnancy and Lactation with Cow's Milk Fortified with Concentrate of Cod Liver Oil: (Test on Rachitic Infants and Rats). D. J. Barnes, Frances Cope, Helen A. Hunscher and Iole G. Macy, Detroit.—p. 647.
Inorganic Salts in Nutrition: IX. Correlation Between Suppressed Growth and Development of Polycythemia Induced by Feeding a Ration Poor in Salts. Pearl P. Swanson, Ames, Iowa, and A. H. Smith, New Haven, Conn.—p. 659.
Derivation of Factors for Computing Gaseous Exchange and Heat Production in Metabolism of Casein by Albino Rat. M. Kriss and R. C. Miller, State College, Pa.—p. 669.
Effect of Vitamin A Deficiency on Concentration of Blood Lipids of Albino Rats. Margaret Elizabeth Smith, Fayetteville, Ark.—p. 675.
Relation Between Antirachitic Factor and Weight of Gallbladder and Contents of Chicken. W. C. Russell, M. W. Taylor and D. F. Chichester, New Brunswick, N. J.—p. 689.
Basal Metabolism of European Women in South India and Effect of Change of Climate on European and South Indian Women. Eleanor D. Mason, Madras, India.—p. 695.
Assimilation of Phosphorus from Di-Calcium Phosphate, Chemically Pure, Tri-Calcium Phosphate, Chemically Pure, Bone Di-Calcium Phosphate and Cooked Bonemeal. K. V. Rottensten and L. A. Maynard, Ithaca, N. Y.—p. 715.
Seasonal Variation in Antirachitic Effectiveness of Sunshine. H. J. Sloan, Ithaca, N. Y.—p. 731.

Maine Medical Journal, Portland

25: 241-254 (Dec.) 1934

Progressive Health Work in Public Schools. H. H. Cleveland, Portland.—p. 242.

Medicine, Baltimore

13: 377-504 (Dec.) 1934

The Etiology of Leprosy. E. B. McKinley, Washington, D. C.—p. 377.

New England Journal of Medicine, Boston

211: 1039-1076 (Dec. 6) 1934

One-Stage Operation for Resection of Cecum and Proximal Colon. S. C. Harvey, New Haven, Conn.—p. 1039.
Amebiasis in Boston. G. C. Shattuck, Boston.—p. 1044.
Displacement of Liver. C. W. McClure and H. A. Osgood, Boston.—p. 1045.
Continuous Follow-Up Department of the Modern Hospital. H. A. Nissen, Boston.—p. 1048.
Contribution to Technic of Fat Grafts. F. J. Cotton, Boston.—p. 1051.

Philippine Islands Med. Association Journal, Manila

14: 421-462 (Nov.) 1934

Local Effects of Injection of Iodized Wightiana Ethyl Esters and Wightiana Oil Round Nerve Trunks. J. O. Nolasco, Culion.—p. 421.
Diagnostic Significance of Shoulder Tip Reflex Pain. A. Liboro and J. P. Celis, Manila.—p. 434.
Medical Ethics and the Times: Need for Reform. J. D. Castillo and C. Camomot, Cebu, Cebu.—p. 441.

Virginia Medical Monthly, Richmond

61: 439-502 (Nov.) 1934

Medicine an Art and a Science. R. D. Bates, Newtown.—p. 439.
Some Arterial Disorders of the Brain Complicating General Medical Diseases. A. G. Brown Jr., Richmond.—p. 442.
Treatment of Common Types of Chronic Arthritis. T. P. Sprunt, Baltimore.—p. 448.
Treatment of Pneumonia with Serums and Immunogens: Case Reports. M. C. Newton, Narrows.—p. 456.
Classification and Etiology of Heart Disease. L. E. Stubbs, Newport News.—p. 458.
Symptoms and Signs of Cardiac Failure. P. F. Whitaker, Kinston, N. C.—p. 461.
Calcium Ortho-Iodoxybenzoate in Treatment of Arthritis. T. Wheeldon, Richmond.—p. 465.

61: 503-564 (Dec.) 1934

The General Practitioners' Interest in Rectal Diseases. H. B. Stone, Baltimore.—p. 503.
Injection Treatment of Acute Thrombophlebitis in Varicose Veins. E. L. Lowenberg, Norfolk.—p. 510.
Management of Heterophoria. J. H. Dunnington, New York.—p. 515.
Significance of Neisserian Smears from the Prostate and Seminal Vesicles: Preliminary Report. W. M. Bowman, Petersburg.—p. 519.
Tumor of the Kidney, with Especial Reference to Too Frequent Disregard of Its Chief Clinical Manifestation. J. F. Geisinger, Richmond.—p. 522.
*Milk Sickness. Ronda Horton Hardin, Banner Elk, N. C.—p. 528.
Clinic Obstetrics: Review of Fifty-Two Consecutive Cases. R. B. Nichella, Norfolk.—p. 531.
Accidental Pneumocranium. J. P. Madigan, Washington, D. C.—p. 536.
Skin Eruption with Codeine: Case Report. M. H. Harris, West Point.—p. 537.
Purulent Pericarditis: Case Report. H. Davis, Roanoke.—p. 539.

Milk Sickness.—Hardin has seen this disease for the last sixteen years and has treated more than 100 cases. Alcohol seems to have an affinity for the substance causing the disease and there seems to be nothing better as an antidote than alcohol pushed to the point of intoxication. She also finds that gastric lavage, duodenal drainage, hypodermoclysis of physiologic solution of sodium chloride and dextrose work extremely well. A majority of patients treated without alcohol in some form or other usually die. The custom of the mountaineers treating it with brandy and honey cannot be dismissed lightly. No difference has been found in the effect of brandy and any other type of alcohol. In man, the principal symptoms are loss of appetite, constipation, pain and stiffness in the legs, languor, fatigue, nausea and vomiting (which may be continuous), the tongue is red, the breath smells of acetone, the temperature is subnormal and the blood pressure is low. There is a lump or heaviness felt in the pit of the stomach, which is not relieved by vomiting and is felt until the patient is well. Overheating or violent exercise will bring about an acute stage of the disease, as it does in animals.

West Virginia Medical Journal, Charleston

30: 529-576 (Dec.) 1934

The Problem of the Cross-Eyed Child. L. C. Peter, Philadelphia.—p. 529.
Sane Hospitalization and Treatment of the Insane. J. E. Offner, Weston.—p. 534.
Review of Etiology and Pathology of Various Cardiac Conditions. C. C. Fenton, Morgantown.—p. 539.
Collapse Therapy in Treatment of Pulmonary Tuberculosis. G. L. Leslie, Howell, Mich.—p. 543.
Syphilitic Hemiplegia: Report of Case. W. D. Fitzhugh and P. R. Fox, McComas.—p. 548.
Sinusitis and Its Complications with Few Related Dental Problems. Sobisca S. Hall and H. V. Thomas, Fairmont.—p. 550.
Strophanthus. E. Podolsky, Brooklyn.—p. 560.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Medical Journal, London

2: 891-928 (Nov. 17) 1934

Some Aspects of Pain. M. Critchley.—p. 891.
Physical Efficiency After Operations for Hernia. C. M. Page.—p. 896.
*Prolapse Syndrome. A. C. Palmer.—p. 899.
Cyclopropane Anesthesia. W. S. Sykes.—p. 901.

Prolapse Syndrome.—Palmer combines the operative procedures of anterior colporrhaphy, vaginal hysterectomy, reconstruction of the hernia of the pouch of Douglas, posterior colporrhaphy and perineorrhaphy for the prolapse syndrome. The operative field is prepared and the perineum is incised back to the anal margin. The nymphae are sutured to the thighs, and traction sutures are inserted in the cervix. The area of vaginal mucosa to be removed is determined: (1) of the anterior mucosa; a landmark suture is inserted to mark the upper end of the new anterior vaginal wall, and (2) of the posterior vaginal mucosa; landmark sutures are inserted at the site of the upper end of the new posterior vaginal wall. The redundant tissue of the anterior and posterior mucosa and the uterus is removed in one technic. In reconstructing the pelvic diaphragm, the uterine stumps and ovariopelvic stumps are fixed on either side to the upper margin of the new lateral vaginal walls. The cut edge of the peritoneum of the uterovesical pouch are joined to the anterior landmark sutures, thus forming the upper end of the new anterior vaginal wall. The anterior vaginal wall is reconstructed. The redundant peritoneum of the hernia of the pouch of Douglas is removed and the peritoneal stumps are sutured to the posterior landmark sutures, thus forming the upper end of the new posterior vaginal wall. The posterior vaginal mucosa and the perineal body are reconstructed. The author states that the operation requires an hour to an hour and fifteen minutes for its performance, without undue difficulty in the control of unexpected oozing. There is, as a rule, no appreciable shock, and the patients do not have a stormy postoperative period. In general they are sitting up the next day, ready to do justice to their dinner. Toward the end of a week there is usually some vaginal discharge, which clears up readily with douching. The length of stay in the hospital and the convalescent period are the same as that for simple repair operations.

Indian Medical Gazette, Calcutta

69: 541-600 (Oct.) 1934

Latent Malarial Infection in Monkeys. R. Knowles and B. M. Das Gupta.—p. 541.
Clinical Study of Climatic Bubo and Allied Conditions. R. V. Rajam.—p. 546.
Filarial Affections of the Male Genital Tracts. P. N. Ray.—p. 554.
Streptococcic Septicemia and Filarial Orchitis. M. N. De and K. D. Chatterjee.—p. 558.
*Concentration of Quinine in Blood After Intravenous and Intramuscular Injections. R. N. Chopra, A. C. Roy and B. M. Das Gupta.—p. 560.
Quinine in Therapeutics of Malaria. R. A. Murphy.—p. 566.
Early Treatment of Malaria. H. Williamson and S. Singh.—p. 568.
Intravenous Quinine Therapy in Malaria. S. Subrahmanyam.—p. 570.
Intravenous Versus Intramuscular Quinine: Notes. D. Manson.—p. 571.
*Some Observations on Combined Method of Clot Culture and Widal Reaction, and on Prognostic Significance of Small Flaking or O Agglutinins in Typhoid Fever. D. W. Soman.—p. 572.
Some Observations After Splenectomy in Rabbits. R. K. Pal, S. Prasad and H. N. Banerjee.—p. 577.

Concentration of Quinine in Blood After Intravenous and Intramuscular Injections.—The experiments of Chopra and his associates on monkeys show that, if allowance is made for small variations due to the constantly changing factors in the animal organism, the concentration of quinine in the blood after administration by the oral and parenteral routes runs almost parallel. In some cases the concentration obtained within the first few hours after oral administration was definitely smaller, but the concentration soon rose to practically the level of the parenteral routes. In ordinary cases no great advantage can be claimed for any particular method. The routes selected by the clinician should therefore be what suits the patient best. The clinical condition of the patient is the best guide in deciding what route should be adopted. The oral route is undoubtedly the method of choice in the vast majority of cases. The condition of the tongue is an excellent indication of the state of the

gastric mucosa; in ordinary attacks of malarial fever the tongue is moist and slightly furred and under these circumstances quinine is absorbed very well from the intestine. If the tongue is dry, red and cracked, quinine is absorbed badly and in such cases other means should be adopted. Quinine is generally absorbed readily from the intestine; even in cases of severe malaria complicated by dysentery, quinine has been shown to be absorbed. In those cases, however, in which there is nausea and vomiting, or when the bilious vomiting of malignant tertian infection is present, it is useless to give quinine orally and the parenteral routes should be adopted, the intravenous or the intramuscular route being selected according to the requirements of the patient. As soon as the condition of the gastro-intestinal tract improves, administration by the parenteral routes should be stopped and the drug should be given orally. In view of the possible injury to the blood vessels, muscles, nerves and so on by parenteral injections, this method should not be used for routine treatment of malaria but is especially indicated in acute cases of severe type for as long as the emergency lasts.

Prognostic Significance of Small Flaking or O Agglutinins in Typhoid.—Soman states that somatic agglutinins play an important part in the immunology of enteric fevers, and particularly in typhoid. By estimation of the titer during the course of the infection, at critical junctures in the clinical prognosis it is possible to forecast with considerable accuracy the chances of life. It is essential to consider the results of the O Widal test and the clot culture together from the same sample in interpreting the significance of the presence or absence of O agglutinins. Their absence in the second week, combined with the presence of the causative organism in the blood, should arouse grave suspicion as regards the immunologic response of the patient. Absence of O agglutinins in the third week of typhoid with a negative clot culture may be looked on as a natural termination of events. Small flaking or O agglutinins play an inconspicuous part in the serodiagnosis of typhoid, especially in Bombay, and therefore it appears unnecessary to make use of the O agglutination test as a routine measure, provided the combined method of clot culture and H agglutination test is done from the same sample of blood. The incidence of inoculated cases also being small, as compared with other advanced countries, there is little chance of discrepancies in the Widal test by the method of Dreyer. Even in inoculated persons suffering from typhoid it is advisable to follow this combined method of clot culture and Widal test, as then the clot culture will settle the diagnosis irrespective of O and H agglutinins.

Journal of Pathology and Bacteriology, Edinburgh

39: 551-736 (Nov.) 1934

Further Investigations on Gravia, Mitis and Intermediate Types of Corynebacterium Diphtheriae: Type Stability. D. T. Robinson.—p. 551.
Some Effects of Adrenalectomy in Male Rats. S. L. Simpson, M. Dennison and V. Korenchevsky.—p. 569.
Hemangioblastoma of the Adrenal Gland. T. B. Menon and D. R. Annamalai.—p. 591.
*Direct Demonstraton of Anticancer Bodies in Serum of Animals Immune to Homologous Tumor. T. Lumsden, T. F. Macrae and E. Skipper.—p. 595.
*Further Investigations on Bactericidal Properties of Adrenal Extracts. J. Gordon and J. C. Knox.—p. 609.
Complete Male Pseudohermaphroditism with Intra-Abdominal Teratoma Testis. R. Carmichael and C. Oldfield.—p. 617.
Renal Neoplasms in Childhood. G. A. McCurdy.—p. 623.
*Interrelations of Corynebacterium Ovis, Corynebacterium Diphtheriae and Certain Diphtheroid Strains Derived from Human Nasopharynx. G. F. Petrie and D. McClean.—p. 635.
Carbohydrate and Nucleoprotein Fractions Isolated from Brucella Group. Lucy E. Topping.—p. 665.
Investigations into Nature of Gelatin Melting Enzymes Formed by Gas Gangrene Bacteria: Importance of Degree of Acidity of Medium for Action of Enzymes. L. E. Walbum and G. C. Reymann.—p. 669.
*Method of Raising and Maintaining Virulence of Influenza Bacilli, with Some Observations on Pathogenic Properties of Virulent Strains. L. Hoyle.—p. 681.
Histologic Studies on Variability of Tubercle Bacillus. W. Pagel.—p. 689.

Anticancer Bodies in Animals Immune to Homologous Tumor.—Lumsden and his associates' investigation suggests that in addition to anticancer bodies there may be other factors underlying homologous immunity. They are convinced that the formation of antimalignant cell bodies is at least an essential factor, if not the only one, in tumor immunity. In each of forty-one immunized rats a high titer of anticancer bodies was demonstrable in the serum at some period between the third and eighth days after the last immunizing inoculation. Since these anticancer bodies are absent from the serums of control normal and tumor rats, it is impossible to resist the inference that their presence is intimately connected with the mechanism of tumor immunity. Their presence and variation in degree in rats with regressing tumors and in rats immunized against normal tissues strengthen this conclusion. The authors' view is that it is the power to produce antibodies rather than their actual presence which is the essential factor in tumor immunity. The antibodies are formed when the immune animal has need of them, for example after an implantation of Jensen rat sarcoma. An immune rat that has not been injected with Jensen rat sarcoma for a period of many weeks has a low titer of antibodies. It is probable that a similar mechanism is the basis of natural tumor immunity. When the blood of an untreated rat of a breed known to be resistant to Jensen rat sarcoma is tested, anticancer bodies are usually not demonstrable. If fragments of a Jensen rat sarcoma are injected into such a rat a tumor appears, but after growing for from five to ten days regression takes place and conjointly anticancer bodies appear in the rat's serum. The significance of the secondary waves of high and low titer is not clear. Probably they depend on several factors, among which the varying amount and frequency of the withdrawals of blood for the tests may be important. Another variable is the proportion of young translucent to more granular and resistant forms of sarcoma cells in the tissue cultures used on a particular day. If many of the young translucent sarcoma cells are present, the titer of the serums tested on that day tends to appear high, since this type of cell is especially sensitive to anticancer bodies.

Bactericidal Properties of Adrenal Extracts.—Gordon and Knox report that an aqueous extract prepared from the adrenal, and especially from the medulla, shows marked bactericidal action on a number of organisms if the extract is exposed to air. Solutions of epinephrine behave in almost the same way and there can be little doubt that partially oxidized epinephrine is the chief active constituent of the bactericidal extracts. Too prolonged exposure to air of either adrenal extracts or epinephrine solutions results in a gradual and almost complete loss of bactericidal power. Inactivation of both extracts and epinephrine solutions can also be effected by the addition of blood or serum, or by slow percolation through a layer of washed permutite. The most sensitive of the organisms tested were Corynebacterium diphtheriae (mitis, gravis and "intermediate") and Vibrio cholerae. Other sensitive organisms were Bacillus anthracis, Staphylococcus aureus and albus, Corynebacterium Hofmannii, Bacillus paratyphosus A and B, Friedländeri, enteritidis (Gaertner), typhosus and dysenteriae (Flexner). Rather less sensitive were Bacillus coli and pyocyaneus, and still less sensitive were Bacillus subtilis and prodigiosus and the streptococci. It is possible, as suggested by Raper, that some substance of the orthoquinone type is produced in the course of the atmospheric oxidation of epinephrine and that this substance is the active bactericidal agent. Morgan and Cooper have shown that several quinones are powerfully bactericidal.

Interrelations of Corynebacterium Ovis, Diphtheriae and Diphtheroid Strains Derived from Human Nasopharynx.—Petrie and McClean state that there is no relationship between the specific toxins that are present in filtrates of broth cultures of Corynebacterium ovis and diphtheriae. An examination of the toxin-antitoxin relations of Corynebacterium diphtheriae, Mair's aberrant strain of Corynebacterium diphtheriae, the group of aberrant diphtheroid strains described by Barratt, and Corynebacterium ovis has shown that these strains possess characters which link them together. The strain discovered by Mair occupies a key position in the group because it has an affinity not only to the typical Corynebacterium diphtheriae but to Corynebacterium ovis and the aberrant diphtheroid strains of Barratt.

Raising the Virulence of Influenza Bacilli.—According to Hoyle, the virulence of many strains of influenza bacilli can be raised and maintained indefinitely by intrapleural passage in rabbits. By the injection of cultures of influenza bacilli of

raised virulence intrapleurally in rabbits a bronchopneumonia can be produced consistently, the lesion having a close resemblance to that of human influenzal pneumonia. The results of intratracheal inoculation of influenza bacilli in rabbits and guinea-pigs would suggest that it is probably not possible to produce a spreading tracheal infection in these animals, and, although occasional animals so inoculated may die of septicemia or bronchopneumonia, it is probable that severe traumatic damage to the lung is essential before such a result can occur. Rabbits and guinea-pigs develop readily a condition of hemorrhagic edema of the lungs as a result of the introduction of liquids intratracheally, so that great caution is necessary in interpreting the significance of pulmonary lesions consequent on such inoculations.

Journal of Tropical Medicine and Hygiene, London

37: 321-336 (Nov. 1) 1934

Acute Articular Rheumatism (Maladie de Bouillaud): Is It Really a Polymicrobic Syndrome? Rôle of Pneumococcus as Specific Agent: Scarlatinal Rheumatism: Treatment of Focal Infection by X-Ray. N. Farah.—p. 321.
Hymenolepis Nana Infection: Case. A. J. Noronha.—p. 325.

37: 337-352 (Nov. 15) 1934

Outbreak of Food Poisoning in Trinidad Due to Bacteria Aertrycke in Tinned Sardines. J. L. Pawan and R. Scheult.—p. 337.
Pathogenesis of Ascariasis. R. Girges.—p. 340.
Acute Articular Rheumatism (Maladie de Bouillaud): Is It Really a Polymicrobic Syndrome? Rôle of Pneumococcus as Specific Agent: Scarlatinal Rheumatism: Treatment of Focal Infection by X-Ray. N. Farah.—p. 343.

Lancet, London

2: 1145-1206 (Nov. 24) 1934

Tremor, Ataxy and Spasm. W. Harris.—p. 1145.
Individual Variation in Response to Drugs. A. J. Clark.—p. 1149.
Surgical Anatomy of Anal Canal, with Especial Reference to Anorectal Fistulas. E. T. C. Milligan and C. N. Morgan.—p. 1150.
Retroperitoneal Hernia: Account of Two Cases. A. E. Porritt.—p. 1156.
Combined Study of Basal Metabolism and Impedance Angle in Thyrotoxicosis and Myxedema. J. D. Robertson and A. T. Wilson.—p. 1158.

Medical Press and Circular, London

189: 453-474 (Nov. 21) 1934

Treatment of Athletic Injuries. R. S. Woods.—p. 456.
*Clinical Features of Hemochromatosis (Bronze Diabetes). J. H. Sheldon.—p. 461.
Availability of Food. R. A. McCance.—p. 463.
Suicide and Euthanasia. F. P. Weber.—p. 466.

Clinical Features of Hemochromatosis.—Sheldon states that the diagnosis of a typical case of hemochromatosis should not give rise to difficulties, once the classic triad of enlargement of the liver, pigmentation of the skin and diabetes is recognized. There will always be latent cases in which one or more of these may be absent, and it is then that difficulties may arise. The diagnosis is most difficult in cases that merely show an enlarged liver, without either pigmentation of the skin or diabetes. In such cases one should always look for the presence of the syndrome of sexual hypoplasia and for an abnormal bluish black pigmentation round the epiglottis and larynx. In addition, the Rous test should be carried out and a biopsy of the skin performed in order to see whether there is a deposit of hemosiderin in the sweat glands and corium. The presence of the latter feature may be taken as pathognomonic. If in addition to the absence of one or more of the major features these subsidiary ones are all lacking, it is unlikely that the case is one of hemochromatosis. The author presents an exception to this statement in a case in which pigmentation of the skin antedated all the other symptoms by a period of years. In such a case the presence of a metallic shade in the pigmentation is suggestive, and, once the characteristic nuance has been seen, it gives certainty. In such cases the final diagnosis can be substantiated only by the passage of time.

South African Medical Journal, Cape Town

8: 781-820 (Nov. 10) 1934

Remarks on Treatment of Syphilis. F. W. F. Purcell.—p. 783.
Breech Presentations. B. D. Knoblauch.—p. 788.
Deep X-Ray Therapy. J. M. Grieve Jr.—p. 789.
The Public Health Aspect of Typhoid Fever. G. D. Laing.—p. 793.
Typhus-like Fevers in the Union of South Africa. W. F. Rhodes.—p. 797.

Gynécologie et Obstétrique, Paris

30: 305-400 (Oct.) 1934

*Does Elevated Value of Gonad Stimulating Factor in Urine of Pregnant Women Always Indicate Hydatiform Mole? Reeb, Nerson and Klein.—p. 305.
Technic of Implantation of Ureters in Large Intestine. N. Markoff.—p. 316.
Study of Prognosis and Treatment of Frontal Presentation. A. S ovall.—p. 326.
Torsion of Pedicle of Cystic Tumors of Ovary. B. I. Seibile.—p. 352.

Gonad Stimulating Factor in Urine and Hydatiform Mole.—Reeb and his collaborators believe that cases already reported prove that the value of the gonad stimulating factor in the urine of pregnant women is not necessarily always increased even in the presence of a living hydatiform mole. Whether the reverse is true—that it is possible to have an increased value of the gonad stimulating factor in the urine without the presence of a mole—is the subject of their report. Two cases are reported by them. In both pregnant women the uterus was too large to correspond with the last menstrual period; there were repeated hemorrhages for from eight to ten weeks, a negative roentgenogram in one case, the absence of albumin in the urine and toxic signs, but there was a highly elevated value of the gonad stimulating factor in the urine. The strong presumptive evidence of hydatiform mole and the necessity of stopping the loss of blood gave sufficient indication for evacuation of the uterus. Actually no hydatiform mole was present, but histologic examination of the placentas showed an exaggerated activity of the ectodermal covering of the villosities of molar character in one case, and a less marked but also abnormal condition in the other. The authors believe that this exuberance of the plasmodes of the Langhans cells, which is not normally seen in placentas of the fourth or fifth month, probably explains the elevated values of the gonad stimulating factor in the urine.

Presse Médicale, Paris

42: 1809-1876 (Nov. 17) 1934. Partial Index

Scarring Syphilids and Gangrenous Syphilids. G. Milian.—p. 1816.
Volkmann's Syndrome Treated by Arteriectomy: Histologic Study of Obliterated Humoral Artery. P. Mathieu, P. Padovani, R. Letulle and P. Normand.—p. 1819.
Progressive Ossifying Myositis. F. Masselot, A. Jaubert de Beaujeu and E. Bloch.—p. 1823.
*Researches on Dissociation of Tubercle Bacillus. A. Saenz and L. Costil.—p. 1827.
Solitary Pediculated Adenoma of Liver. C. Lenormant, I. Bertrand and J. Patel.—p. 1829.
Ollier's Chondrodysplasia. A. Richard, P. V. Dupuis, C. Rœderer and R. Froyez.—p. 1833.
Bundle of His: Its Ventricular Connections. E. Gérauriel.—p. 1854.
Some Results of Arteriography in Arterial Diseases and Tumors. X.-J. Contiades and J. Naulleau.—p. 1866.
Function of Spleen: Its Diagnostic Importance. P. Émile-Weil and P. Isch-Wall.—p. 1874.

Dissociation of Tubercle Bacillus.—As a result of cultural and animal experiments, Saenz and Costil conclude that stocks of tubercle bacilli of mammals may be easily dissociated into two types of colonies. The S variant is non-tubercle forming and causes inflammatory lesions in the guinea-pig, rabbit and hen, which recover when small doses are given, while the R variant, with the exception of B C G, which never produces lesions of generalized tuberculosis, is tubercle forming and produces generalized lesions. They succeeded in transforming the R variant of the avian bacillus into S, and vice versa. Glycerinized potato, for example, is favorable for the slow transformation of S into R. They conclude, therefore, that the attenuation of virulence of strains of avian bacilli long kept in the laboratories is due to the fact that the initial variant S, which always predominates in freshly isolated cultures, is replaced by the variant R, which is much less pathogenic and whose morphologic characteristics approach that of the bacilli of mammals. The dissociation of human strains was more laborious and it was difficult to obtain several variants. The pigmentation of the chromogenic variant was less intense than that of the avian and was observed only in the colonies of the S variant. The authors believe that their observations on dissociation indicate that all types or varieties of tubercle bacilli are derived from a single primitive stock. The elements of this common specific stock, in accomplishing their evolution in one or another sensitive animal, give rise to the bacillary

elements of the S variant and terminate in greater and greater predominance of the elements of the R variant. It is by reason of this adaptation that the avian bacillus, represented essentially by the S variant, is the most primitive and least differentiated type. The bovine type comes next. The human type, on the contrary, in which the R variant predominates, is the most narrowly adapted. These facts and conclusions, they believe, throw a new light on microbiologic and clinical facts heretofore difficult to explain.

Prensa Médica Argentina, Buenos Aires

21: 2049-2098 (Oct. 31) 1934

Intestinal Amebiasis: Clinical and Parasitologic Study of Twenty-Seven Hundred Cases. M. R. Castex and D. Greenway.—p. 2049.
Teaching of Medicine. B. A. Houssay.—p. 2070.
Conservative Surgery in Gynecology: Indications and Results. C. R. Cirio and E. G. Murray.—p. 2078.
*Temporary Sterilization by Biologic Method. M. Schteingart and A. G. Peralta Ramos.—p. 2087.
Acute Encephalitis with Pyramidal Symptoms and Typical Mental Confusion: Case Ending on Recovery. J. M. Macera, J. Pereyra Kafer and B. A. Messina.—p. 2089.

Temporary Sterilization by Biologic Method.—Schteingart and Peralta Ramos obtained satisfactory results in 80 per cent of their cases by the administration of four subcutaneous injections of dead spermatozoa of sheep, given at intervals of two days. The first injection contains thirty million dead spermatozoa, the second twice as many as the first, the third twice as many as the second, and so on in multiple proportions. Neither local nor general reactions, worthy of consideration, are observable. The injections of large doses of spermatozoa do not alter the results. When the treatment is given for the first time it produces sterilization for from six to fifteen months, but the duration of sterility becomes shorter as the treatments go on. Conception is resumed under normal conditions whether the treatment has been given one or more times.

Semana Médica, Buenos Aires

41: 1553-1660 (Nov. 22) 1934. Partial Index

Dermoid Fistulas and Cysts of Coccigeal Region. R. C. Ferrari.—p. 1553.
Salivary Crises in Tabes: Case. J. C. Montanaro and J. L. Hanón.—p. 1619.
*Puberal Goiters. E. B. del Castillo and J. Argonz.—p. 1625.
Red Myoma in Pregnancy: Case. J. León and D. E. Caravias.—p. 1636.
Open Articular Fractures: Treatment with Early Suture Without Drainage. T. Gioia.—p. 1642.

Goiters at Puberty.—Del Castillo and Argonz say that different types of goiter (even those of the type of toxic adenoma) are observed at puberty. The prognosis of hyperthyroidism is more serious at puberty than if the condition appears during the adult age. The articles reported on the functional interrelationship between the anterior lobe of the hypophysis, the gonads and the thyroid are of importance. The origin of puberal colloid goiter may be traced to a scanty content of iodine in drinking water if the patients live in the mountains, and to an excess if they live on the prairies. Puberal goiter should be classified, according to the variations of the basal metabolism, in the following types: (1) goiter with normal basal metabolism (colloid type), (2) goiter with increased basal metabolism (type of toxic adenoma) and (3) goiter with decreased basal metabolism (type of thyroid insufficiency without myxedema).

Archiv für Gynäkologie, Berlin

158: 321-504 (Nov. 23) 1934. Partial Index

Treatment of Eclampsia. W. Stroganoff.—p. 321.
Membranous Dysmenorrhea, an Incretory Disorder. A. Pohl.—p. 326.
*Glycogen in Placenta. H. Guthmann and Leonie Böhme.—p. 336.
Corpus Luteum Hormone and Its Demonstration in Pure Form. E. Fels.—p. 364.
*Theory and Practice of Determination of Sex. P. H. Schumacher.—p. 393.
Quantity, Distribution and Significance of Placental Glycogen in Various Phases of Pregnancy. B. Szendi.—p. 409.

Glycogen in Placenta.—Guthmann and Böhme examined surgical specimens for the glycogen content of the fetal and maternal portions of the placenta during the different months of the gestation period. They found that the glycogen content in the maternal portion decreases as the pregnancy progresses, while in the fetal portion the opposite is the case. With the exception of the blood corpuscles, particularly the leukocytes and lymphocytes, glycogen is present in all the cells of the placenta, but there are sites of predilection. In the maternal portion the decidua and the adhering portions of the uterine mucous membrane contain the largest amounts of glycogen, while in the fetal portion the glycogen is present in large quantities in the layer of Langhans. The syncytium contains little glycogen, the stroma more. In the stroma there are two different types of deposits, those of the connective tissue and those of the lymph channels. In this manner the arrangement of the glycogen is linear in the villi. The placental vessels contain from the beginning, particularly in the muscle portions and the connective tissue portions, considerable amounts of glycogen, and they increase further with advancing pregnancy. A direct transfer of the glycogen in the maternal tissue to the fetal tissue was not demonstrable; thus the transfer may have taken place only by resynthesis.

Determination of Sex of Offspring.—Schumacher evaluates the various theories of the determination of the sex of the offspring. He shows that the theory accepted by Hippocrates and Galen, namely, that the products of the gonads of one side produce male and of those of the other side female offspring, have been disproved by the fact that in unilateral castration children of both sexes have been born. The dietetic hypotheses, according to which the diet of the mother exerts an influence on the sex of the offspring, could not be corroborated. The influence of the age of the parents on the sex of the offspring is, if present at all, so slight that it is of no practical significance. Siegel's theory, that the fertilization of young ova produces girls and the fertilization of old ova boys, does not correspond to the present knowledge about the duration of the viability of the ovum and the sex determining factors of the spermatozoa. The influence exerted by the term of cohabitation on the incidence of male and female births is still in dispute. Modern hereditary science and zoology maintain that the sex of the fetus is determined by the spermatozoa, stating that there are male and female spermatozoa, but only one type of ova. The author investigated the observations of Unterberger (*Deutsche med. Wchnschr.* **56:**304 [Feb. 21] 1930; abstr., THE JOURNAL, May 3, 1930, p. 1451), that alkalinization of the vaginal secretion would produce male offspring. However, his studies on human subjects or on animals did not corroborate Unterberger's work. Moreover, the author considers the use of this method inadvisable in human subjects, since the chemical alteration of the vaginal secretion may result in an impairment of the offspring. The attempt to modify the sex of the fetus by treating the mother with sex hormones has so far only theoretical interest. The author is conducting experiments for the clarification of this problem.

Archiv für Kinderheilkunde, Stuttgart

103: 193-256 (Nov. 23) 1934. Partial Index

Diastasis Recti Abdominis During Childhood. R. Fischl.—p. 193.
Aspects of Aphthous Stomatitis. P. von Gara and W. Hertz.—p. 204.
*Hanganatziu-Deicher Reaction During Childhood. P. Dudäs.—p. 214.
*"Focal Reactions" in Diphtheria Allergy. J. Siegl.—p. 223.
Erythema Nodosum and Scarlet Fever. D. von Moritz.—p. 227.
Studies on Relief of Colon in Nurslings. K. Gefferth.—p. 231.

Hanganatziu-Deicher Reaction During Childhood.—Dudäs points out that Hanganatziu and, independent of him, Deicher observed that, following the parenteral administration of heterogenic serum, human blood serum agglutinates certain heterogenic erythrocytes, particularly those of sheep, horses, hares and guinea-pigs. Especially noteworthy is the high agglutination titer toward the erythrocytes of sheep after the person has received horse serum parenterally. Other authors found that the Hanganatziu-Deicher reaction is strongly positive, particularly in monocytic angina. Dudäs studied the Hanganatziu-Deicher reaction in nurslings and children. The test was made as follows: To 1 cc. of serum, inactivated by heating for fifteen minutes in a water bath at 56 C., 1 cc. of physiologic solution of sodium chloride is added. Then 1 cc. of this mixture is withdrawn and placed in another test tube, which contains already 1 cc. of physiologic solution of sodium chloride, and the series is continued in this manner. Now 0.5 cc. of fluid is removed from each tube and is replaced by 0.5 cc. of a 5 per cent suspension of sheep corpuscles. Finally 1 cc. of physiologic solution of sodium chloride is put into each tube

so that they all contain 2 cc. of fluid. After the contents have been mixed thoroughly the whole series is placed in the incubator for two hours and then for twenty-four hours in the icebox. The results are read on the following day. If the agglutination is visible with the naked eye the agglutination is marked ++, whereas microscopic agglutination is marked +. The reaction is considered positive if agglutination is perceptible in a dilution of 1:8 and higher. Cases in which only the dilutions of 1:4 and 1:8 disclosed agglutination were considered as borderline cases. The author found that, following the parenteral administration of serum and following serum disease, the Hanganatziu-Deicher reaction is positive. The reaction becomes positive from eight to ten days following the administration of serum and may remain positive for several months. During measles, after smallpox vaccination, and during the exanthem caused by the sodium salt of phenyl-ethyl-hydantoin, the Hanganatziu-Deicher reaction is positive. The parenteral administration of human blood influences the organism in the positive direction.

"Focal Reactions" in Diphtheria Allergy.—Siegl maintains that it must be considered as proved that in the process of immunization against diphtheria there develops, in addition to the diphtheria antitoxin, also an allergic alteration of the reaction capacity. The positive reactions that develop on the basis of such an allergic condition have, of course, no connection with a specific diphtheria allergy; however, in their appearance and course they greatly resemble those of specific origin, and consequently it is difficult to differentiate them. In a former report (*Arch. f. Kinderh.* **98**:1 [No. 1-2] 1932) he described a method that permits a differentiation of such reactions. He describes here a new allergic phenomenon. He observed that if children who had been given inunctions with Löwenstein's prophylactic diphtheria ointment were given a toxoid injection there developed twenty-four hours after the injection not only a local reaction at the site of the injection and perhaps an increase in temperature but also a large maculopapular exanthem that covered only the region of the inunction with the diphtheria ointment, whereas the other portions of the skin remained free from it. This localization proves the connection with the previous inunctions. The cutaneous reaction is of comparatively short duration, for after forty-eight hours it has either completely disappeared or only slight traces remain. The author considers the phenomenon a flare-up reaction due to the local immunologic processes produced by the toxoid in the prophylactic ointment. These focal changes are in the beginning invisible and become manifest as the result of the toxoid injection. The phenomenon was observed in three out of seventeen children who had been given a toxoid injection after inunction with prophylactic diphtheria ointment. The author describes the histories of these children. The intervals between the last inunction and the toxoid injection causing the reaction were two, eight and fourteen days. In one of the cases only one inunction had been made. Another injection of toxoid, eight days later, did not cause a new flare-up reaction. The author emphasizes that the elicitability of a toxoid flare-up reaction has no connection with tuberculin susceptibility.

Archiv für Verdauungs-Krankheiten, Berlin

54: 237-354 (Nov.) 1934. Partial Index

Quantitative Spectroscopic Method for Examination of Porphyrin. K. Lageder.—p. 237.
*Results of "Protein Body Therapy" in Gastric and Duodenal Ulcer. A. Engel.—p. 256.
*Diet Containing Flour of Soy Beans in Treatment of Suppurating Urinary Infections, Eczema and Diabetes. C. Becker.—p. 260.
Basal Metabolism and Specific Dynamic Action in Obesity. H. Rothschild.—p. 279.
Refractometric Studies on Bile. S. Cserna, K. Engel and T. Epstein.—p. 307.
Gastro-Intestinal Disturbances in Addison's Disease. K. Herman.—p. 312.

Protein Therapy in Gastric and Duodenal Ulcer.—Engel describes his observations on protein therapy of gastric ulcer in seventy cases in which an ulcer had been demonstrated by roentgenoscopy, gastroscopy or clinical examination. Cases presenting adhesions, severe stenosis or nervous disturbances have been excluded from the protein therapy. The injections of the protein preparation were begun after dietetic treatment had failed. The injections were made intravenously, beginning with doses of from 0.2 to 0.4 cc. and gradually increasing to 1 or 2 cc. They were given at intervals of from three to four days. A series consisted of from four to eight or, rarely, twelve injections. In almost half of the cases a slight increase in temperature resulted from the injections. High fever, necessitating interruption of the injections, developed in two cases. Local reactions in the form of gastric pains and increased hemorrhages were not observed. In the majority of cases the gastric pains decreased after the first injections. At the same time the weight of the patients increased and in some cases the roentgenogram revealed improvement. Complete cure was effected in 19 per cent of the cases; great improvement, that is, complete freedom from symptoms, was observed in an additional 39 per cent of the cases; slight improvement was noted in 30 per cent of the cases, and in only 12 per cent was the protein therapy a complete failure. These results compare favorably with those of other therapeutic methods, and the author thinks that ulcers which do not yield to dietetic treatment should be subjected to protein therapy before surgical treatment is resorted to.

Soy Flour in Treatment of Urinary Infections, Eczema and Diabetes.—In an analysis of various flours, Becker shows that soy flour differs from other flours in that it is rich in proteins and fats and almost free from starch. The carbohydrates of soy flour appear in the form of soluble saccharose, and the flour contains large amounts of lipoid (lecithin) and minerals. Because of this composition, the soy flour has therapeutic value in urinary infections, eczema and diabetes. Its action is due to the large quantities of bases it provides for the organism, for the high mineral content of the soy bean increases the alkalinity of the urine within a short time to a p_H of 8.4 and more. This alkalotic alteration is already effective in the internal metabolism and is not caused by ammonia cleavage of the urea in the urine by urease, a ferment of the soy bean. The large amount of minerals and a number of other substances contained in the soy bean effect in eczema a reduction in the inflammatory process and protect the overtaxed peripheral capillaries. Moreover, by providing a high caloric food of plant origin and thus permitting the exclusion of animal foods, particularly milk, the allergic factor is largely excluded in the eczemas of nurslings and children. The anti-inflammatory action and the alkalinization of the urine, which in turn restricts the growth of colon bacilli, are the effective factors in pyuria. In diabetes the basic salts of the soy bean neutralize the excessive organic acids and thus reduce the acidosis. Bread prepared from soy flour is an adequate substitute for wheat bread in the diet of patients with diabetes mellitus. The use of this bread in the diet reduces glycosuria and also the blood sugar values.

Deutsche Zeitschrift für Chirurgie, Berlin

244: 1-100 (Nov. 22) 1934

*Contribution to Knowledge of Exophthalmic Goiter. O. Voss.—p. 1.
Symptomatology and Pathology of Giant Cell Tumors of Tendon Sheaths. W. Hetzar.—p. 63.
Contribution to Malignant Tumors of Thyroid. D. A. Mulvihill.—p. 71.
Genesis of Distant Thrombosis. K. Lenggenhager.—p. 77.
Symptomatology of Congenital Struma. L. von Unterrichter.—p. 88.

Exophthalmic Goiter.—According to Voss, iodothyroglobulin is the specific secretion of the thyroid, since it is the only substance so far isolated capable of producing all the symptoms caused by the administration of the thyroid substance itself. Thyroxine is only one of its main constituents. Thyroxine and di-iodothyrosin are the essential constituents of the thyroid secretion. They combine in the thyroid with an albumin to form iodothyroglobulin. Di-iodothyrosin exerts a depressive effect on the action of thyroxine. The author examined thyroid secretions from normal and diseased thyroids with the aid of a spectrograph to determine whether there exist differences in the light absorption, thus demonstrating structural changes in the molecule. Iodothyroglobulin obtained by the method of Oswald from normal thyroids, from goitrous thyroids and from exophthalmic thyroids were submitted to spectrographic examination. No difference was noted in the light absorption by the iodothyroglobulin obtained from normal thyroids and from colloid goiters. The curve representing the light absorption of the secretion from exophthalmic thyroids was

different from that of normal thyroids and of colloid goiters. This suggests that the molecular structure of the iodothyroglobulin of an exophthalmic thyroid differs from that of the normal thyroid and from that of a colloid goiter. Ordinary hyperfunction of the thyroid is easily demonstrable both in clinical cases and in experiment. The question of whether ordinary hyperthyroidism can develop into a genuine exophthalmic goiter has not been answered. The present concept is that the difference in the two forms depends on the rate of evolution, in the course of which a mere hyperfunction passes into a state of dysfunction. Histologically pure hyperthyroidism is represented by a hypertrophy of all the anatomic elements of the gland, including the colloid. In exophthalmic goiter, on the other hand, the colloid is greatly diminished and the epithelium undergoes a characteristic hyperplasia. At present there exist many cases in which, owing to administration of iodine, the typical alterations in the colloid and in the epithelium cannot be demonstrated. The author admits that there are mixed cases in which both the histologic characters of hyperfunction and of exophthalmic goiter exist side by side. The clinical manifestations of hyperthyroidism may be duplicated by thyroid feedings. The symptoms common to the two are tremors, rise in basal metabolic rate, loss of weight, irregular heart action, hypertrophy and degeneration of the heart muscle. Exophthalmos is not present. The characteristic symptoms of exophthalmic goiter cannot be reproduced by thyroid feeding; this applies particularly to such symptoms as exophthalmos and increased vascularity of the gland as evidenced by bruit over the vessels of the gland. The onset is more acute and all the symptoms are more pronounced in exophthalmic goiter. The author found that, whereas chronaxy in normal people is twice as long in extensors as in the flexors, this relationship is disturbed in exophthalmic goiter. On the basis of his experiments the author differentiates between exophthalmic goiter and hyperthyroidism. He assumes that the first is caused by dysfunction of the thyroid while the second is caused by hyperfunction.

Frankfurter Zeitschrift für Pathologie, Munich

47: 313-428 (Nov. 22) 1934. Partial Index

*Acute Miliary Tuberculosis Following Curettage in Tuberculous Endometritis. W. Büngeler.—p. 313.
Nonpigmented Melanoma (Naevocytoblastoma) of Skin. A. Symeonidis.—p. 323.
Chronic Periarteritis Nodosa. E.-E. Bauhe and H. H. Kalbfleisch.—p. 340.
Calcified Necrosis of Suprarenals. R. Goldstein.—p. 360.
*Primary Melanosarcoma of Brain, Pigmented Nevi of Skin, Extensive Neurofibromatosis of Cutaneous Nerves. M. Björneboe.—p. 363.
Typical Mixed Salivary Gland Tumor on Finger. G. Gaehtgens.—p. 374.
*Examination of Urinary and Biliary Calculi in Ultraviolet Rays. V Faber.—p. 421.

Miliary Tuberculosis Following Curettage.—Büngeler describes a case of tuberculous endometritis that developed following an exploratory curettage. A woman, aged 28, had given birth to a living child in 1932. In August 1933 she had an inflammation of the ovaries and in December she complained of pains in the abdomen and of occasional hemorrhages. The family physician diagnosed a pregnancy in the fourth month. In January the woman had an abortion, but the physician was not consulted until two days later, when she developed fever. The physican scraped the uterus with a dull curet, but the material obtained was not examined. Following this curettage, the woman developed a parametritis and since this time her temperature was always increased. An exacerbation occurred at the end of February and the patient died several weeks later. Postmortem examination revealed a caseous tuberculosis of both uterine tubes, tuberculosis of the mucosa of the uterus, numerous tubercles in the intima of the small vessels of the endometrium, a few tubercles in the intima of the ovarian vein, acute miliary tuberculosis, tuberculous meningitis, miliary tuberculosis of the lungs and spleen, disseminated small-noduled tuberculosis of the peritoneum, multiple tubercles in the kidneys and the liver, and dilatation of the entire heart. The increase in temperature following curettage indicates, the author says, that this intervention was made on a uterus already infected with tuberculosis, and the curettage led to a massive invasion of the blood stream by tubercle bacilli. The author shows that the case corroborates the opinion expressed by Ribbert and Huebschmann, who stated that the vascular tubercle is insignificant in the hematogenic dissemination of tuberculosis. The lack of generalized infection of the organism with tuberculous virus in case of genital tuberculosis also seems to play an important part in the development of miliary tuberculosis. The author emphasizes that, if uterine tuberculosis is certain, curettage should never be resorted to.

Melanosarcoma of Brain, Pigmented Nevi of Skin, and Neurofibromatosis of Cutaneous Nerves.—Björneboe says that the concurrence of these three disorders is rare. The patient, a man aged 37, died with symptoms that indicated a rapidly growing cerebral tumor. Postmortem examination revealed a melanosarcoma in the right cerebral hemisphere. On the face and the upper and lower extremities there were numerous brown spots, many of them with hair growth and only partly elevated above the level of the skin. The trunk and the upper extremities had a furlike hair growth, which was sharply and symmetrically defined on the chest. Over the gluteal muscles the skin showed changes indicative of elephantiasis. The skin showed two anomalies—nevi and neurofibromatosis—and the problem is whether these two conditions are related. The concurrence of extensive nevi of the skin and of the neurofibromatosis of the cutaneous nerves in the nevi has been described by Berblinger. The concurrence of Recklinghausen's disease and of cutaneous nevi has been reported repeatedly, particularly by Masson, who maintained that the cells of a nevus are connected with the cells of the Wagner-Meissner tactile bodies. He considers the piles of nevus cells as syncytia that are connected below with nerves and above with cells of the epidermis. These syncytial structures frequently assume forms that resemble the Wagner-Meissner bodies. Masson was able to detect neurofibrils only in the beginning portions of these syncytial structures, but he believed that they were of the same origin as the Wagner-Meissner and the Merckel-Ranvier cells. In attempting to apply this theory to this case, the author was unable to detect neurofibrils in the cutaneous preparations. However, threads were detected that were probably of a nervous nature but had undergone neurofibromatous changes, and it is significant that the threads were partly melanotic. This supports the opinion that the cells are ectodermal (capable of forming pigment). Moreover, this makes it appear likely that the pigmented cells that are located higher up in the cutis are of nervous origin. This one case does not permit a conclusion about the genesis of all nevi. Nevertheless it is a further corroboration of Masson's theory.

Examination of Urinary and Biliary Calculi by Ultraviolet Rays.—Faber observed that urinary and biliary calculi show fluorescence in filtered ultraviolet rays. The urinary calculi showed on exposure to ultraviolet rays a greater number of layers and a more manifold coloration than they did in ordinary light. From the color of the fluorescence it may be concluded of what substances the calculus is composed. The fluorescence of urinary calculi is due to the substances that by adsorption are combined with the salts, which form the calculi. Since bile pigments interfere with fluorescence, it is impossible to deduce conclusions about the composition of biliary calculi from the nature of their fluorescence.

Klinische Wochenschrift, Berlin

13: 1705-1736 (Dec. 1) 1934. Partial Index

Heat Economy and Endocrine System. E. Grafe.—p. 1705.
Cardiac Activity and Sympathetic Poisons: Action of Intravenously Injected Epinephrine and Pilocarpine on Cardiac Action. G. W. Parade and H. R. Foerster.—p. 1709.
*Does Elimination of Corpus Luteum Hormone in Urine Corroborate the Knaus-Ogino Theory of Periodic Fertility and Sterility in Women? E. Glaser and O. Haempel.—p. 1711.
*Serologic Investigations in Multiple Sclerosis. H. Sachs and G. Steiner.—p. 1714.
*Serum Coagulation Reaction of Weltmann in Pulmonary Tuberculosis. Veigtländer.—p. 1718.
Auscultatory Gap. I. Pines and D. Scherf.—p. 1721.
Specific Skin Reaction in Tularemia. W. N. Fjodoroff and H. Goldstern.—p. 1723.

The Corpus Luteum Hormone and Periodic Sterility and Fertility.—Glaser and Haempel describe a method that makes possible a quantitative determination of the corpus luteum hormone in the urine. The urine is subjected to electrodialysis and heat concentration and the substance thus obtained

is tested on female minnows. It was determined that corpus luteum hormone (male hormone), perhaps augmented by hormone of the suprarenal cortex, is present in the urine of women in all stages of the cycle, and also in the urine of young girls and of women of the menopausal age. In young girls and in women of the menopausal age the elimination keeps within comparatively narrow limits, but in the latter certain fluctuations are noticeable, which apparently correspond to the former cycle. In women of the propagative age, the elimination of the female sex hormone is greatest at the time of ovulation, while the largest amounts of corpus luteum hormone (male) are eliminated during the period of menstruation. At this time the daily average is 3,000 fish units. After that its excretion decreases apparently (slower in long cycles, faster in short cycles) until the time of ovulation, and during the last days of the cycle it remains at a daily average of from 300 to 600 fish units. Thus it is impossible to consider the activity of the corpus luteum as restricted to certain periods. A superordinated organ, either the anterior lobe of the hypophysis or a nervous center or both, regulate the elimination. At any rate, the actions of the corpus luteum are rather complicated and cannot be reduced to as simple a system as that suggested by Knaus. The authors believe that the corpus luteum is probably the main cause of the partial failure of the theories of Knaus. They assert that in all stages of the cycle and in all ages the urine contains hormones which promote the growth of the ovipositor of female minnows; however, the elimination is not sufficiently regular to be suitable for test purposes.

Serologic Investigations in Multiple Sclerosis.—Sachs and Steiner admit that the etiology of multiple sclerosis is not fully understood as yet. However, since many investigators are of the opinion that it is the manifestation of an infectious process, the authors felt justified in conducting a search for antibody-like factors in the serum of patients with multiple sclerosis. They employed a complement fixation test and used alcoholic extracts from diseased central organs (brain and spinal cord) as reagents. They gained the impression that the serum of patients with multiple sclerosis actually has a special reactivity to the extracts from brains with multiple sclerosis. They reproduce several tables of the results of their tests, which indicate that there is a noticeable difference in the behavior of the multiple sclerosis serums and the control serums. Moreover, in some patients with multiple sclerosis, who had a positive reaction, a remission in the disease process was followed by a change to a negative reaction. The positive reactions were most frequent during the acute stage of the disorder. In an evaluating summary of their studies the authors show that it is as yet impossible to give a definite estimate of the value of their serologic studies, but their observations so far indicate the existence of a serologic change that is comparatively frequent in patients with multiple sclerosis.

Weltmann's Serum Coagulation Reaction in Tuberculosis.—Voigtländer points out that Weltmann's serum coagulation reaction is helpful in the diagnosis and prognosis of tuberculosis. This new reaction permits a decision as to whether the tuberculous processes in the organism are of the exudative or the fibrous type. He describes the technic of the Weltmann serum coagulation reaction and describes his own experiences with the method. Weltmann had found that a number of febrile processes are accompanied by a narrowing of the coagulation band; that is, by a deviation to the left. That the fever itself was not the cause of the deviation to the left was proved by the fact that in artificially induced fever the flocculation band was normal. Deviation to the left was observed in diseases of inflammatory character (exudation), such as pulmonary tuberculosis, pleurisy with effusion, the acute stage of articular rheumatism, suppurative processes and exudative malignant pulmonary tuberculosis. The coagulation band shows no deviation to the left without an inflammatory, that is, an exudative, process. The degree of deviation runs parallel with the severity of the process. As the inflammatory process improves, the coagulation band returns to normal. A deviation to the right or a widening of the coagulation band was observed by Weltmann in diseases of the hepatic parenchyma, in cardiac decompensation with stasis and in fibrous forms of tuberculosis. The author performed the Weltmann serum coagulation test on 400 inmates of a sanatorium for tuberculous patients and found that the coagulation shows a deviation to the right in fibrous and cirrhotic forms of tuberculosis. In inflammatory processes of pulmonary tuberculosis, in cavernous progressive conditions with exudative processes and in caseous pneumonic pulmonary tuberculosis, a deviation to the left is noticeable. Pulmonary disorders, in which exudative and fibrous processes concur, cannot always be clarified by Weltmann's reaction. In pleural exudates the coagulation band runs practically parallel to the course of the disorder. Since the Weltmann serum coagulation reaction does not always give reliable results, it is advisable to combine it in doubtful cases with the determination of the sedimentation speed of the erythrocytes.

Medizinische Klinik, Berlin

30: 1581-1616 (Nov. 30) 1934

Indications for Surgical and Orthopedic Treatment During Childhood. C. Springer.—p. 1581.
*Influence of Various Metal Compounds on Growth of Bacteria. W. Haase.—p. 1585.
Modern Vitamin Therapy During Childhood. H. Brugsch.—p. 1587.
Coronary Thrombosis. G. Lepehne.—p. 1589.
Drowning: Physiology, Treatment and Accident Evaluation. E. Sehrt. —p. 1591.
Splenomegaly in Traumatic Thrombosis of Splenic Vein. J. Monauni and G. H. Bartsch.—p. 1595.
Alopecia Areata and Hormone Treatment. P. Janson.—p. 1597.

Influence of Metal Compounds on Growth of Bacteria.—Haase tested the foils of copper, brass, tin, aluminum and silver for their bactericidal action and compared it with that of two silver compounds, silver manganite and the silver salt of thiocellobiose. The tests were made with agar plates. The author points out that silver foil has been known as an effective bandage for wounds, but he found that its bactericidal power is rather slight. The foils of other metals exert hardly any bactericidal power on organisms on the agar plate. The silver compounds were found to be much more effective. The silver salt of thiocellobiose was tested with gauze saturated with a 10 per cent solution of the substance. This gauze proved to have great bactericidal power on the agar plate. The author states that the action of this gauze on wounds has not been thoroughly investigated as yet, but, since a 5 per cent solution of the silver salt of thiocellobiose has been used for injection without harmful effects, it may be assumed that wounds will tolerate the gauze impregnated with the substance. In fact, several applications revealed no changes in the course of the development of wounds. Silver manganite proved somewhat less effective on the agar plate than did the silver salt of thiocellobiose; however, it was much more effective than the foils of pure metals. The author points out that silver manganite is introduced into bandage materials, catgut and silver foil and that in this form it finds wide application. It has no irritating effect on wounds and it has been used also in the form of powders and ointments. The author admits that the surface antisepsis of a wound is only a small part in the fight against infection.

Monatsschrift für Kinderheilkunde, Berlin

61: 73-160 (Nov. 27) 1934. Partial Index

*Hormone Regulation of Chloride in Children. G. Török and L. Neufeld. —p. 73.
Action of Parenterally Administered Viosterol in Rachitic Nurslings. S. Liebe.—p. 88.
*Fluctuations in Immunity in Infectious Diseases. G. Meyer zu Hörste. —p. 94.
*Suitability of Roentgen Method for Diagnosis of Appendicitis. H. Kleinschmidt.—p. 115.
Peculiar Combination of Renal Dwarfism with Spastic Diplegia, Idiocy and Atrophy of Optic Nerve (Silberstern's Type). K. Wallis.—p. 121.
Tumors of Suprarenal Medulla During Childhood. F. Eckardt.—p. 127.

Hormone Regulation of Chloride in Children.—Török and Neufeld point out that the action exerted by the hormones of the hypophysis and the thyroid on the chloride-water exchange has been repeatedly investigated but that there are a number of other hormones the action of which on the chloride exchange has not been thoroughly studied as yet, and so they tested a number of these. They made their studies on forty-one children from 5 to 12 years of age. During the first test period the children received at first a standard diet that provided from 5 to 8 Gm. of sodium chloride daily, and then they were put on a milk diet with a lower salt content. During

the second test period, when the children received once more the standard diet, they were given daily injections of hormone or glandular extracts. This period lasted generally eight days and after that the children were put once more on a milk diet. The amount of chloride excreted in the urine was determined daily by the method of Russznyák. The first tests were made with the antidiuretic hormone fraction of the posterior lobe of the hypophysis. During the first part of the second test period, when the antidiuretic posterior hypophyseal hormone was administered daily, the average daily chloride elimination was greater than during the first period, when a standard diet, and no hormone extract, was given. At the time of the milk diet of the second period, an increased retention of chloride was demonstrable. The various sex hormones and extracts were tested on fifteen children. The sex hormone of the anterior hypophysis was tested in four children and the follicle hormone in three; the extract prepared from the entire ovary, the corpus luteum hormone, and the estrus stimulating and inhibiting fractions of the corpus luteum hormone in one child each; the testicular extract in three children, and the extract of the mammary gland in one child. These experiments revealed that, with the exception of the corpus luteum hormone (entire), of the estrus-inhibiting fraction of the corpus luteum and of the mammary hormone, the sex hormones and extracts cause an increased retention of chloride during the time of their administration; but after the administration ceases, the retained chloride is eliminated. The extract of the pineal body was tested in four children. In these tests no regularity was demonstrable. In experiments with extracts of the thymus and the spleen, an increased chloride elimination was noticeable after the administration of these extracts had ceased. While the thymus extract was given, the chloride content of the urine was more or less reduced; but while spleen extract was given, this was not the case, and in one child the elimination was even increased. In the experiments with the tonsillar extract it was found that, although the chloride elimination in the urine was not reduced during the time of the injection of the extract, it increased after the cessation of the injections. The administration of liver extracts proved without influence on the chloride excretion. The same may be said about the extract of the suprarenal cortex and about insulin. Parathyroid extract produced a considerable chloride retention in two children, while in another child, when a less concentrated parathyroid extract was used, this was not the case.

Fluctuations in Immunity in Infectious Diseases.—Meyer zu Hörste points out that the resistance of the organism to infections is subject to considerable fluctuations. It happens, for instance, that the disease suddenly develops in physicians and nurses who for years have worked in a scarlet fever department. But not only the resistance to a certain pathogenic organism but also the so-called natural immunity is subject to fluctuations. In the course of an infectious disease, it may happen that the defense mechanism fails suddenly. In this event a change must take place in the fluids and cells of the organism, which cannot be determined by means of the ordinary methods of examination but may become manifest in the skin or in the visible mucous membranes. The author describes the case of a child, aged 13 months, who developed whooping cough. This became complicated by pneumonia and by cutaneous suppurations in the occiput. Suddenly the condition became more threatening: a meningo-encephalitis and a severe occipital ulceration developed. The child died. This case illustrates the sudden loss of the natural immunity. When this took place, not only did the organism lose resistance to the whooping cough, but the disease processes of the skin likewise did not heal. The author thinks that, when the infectious process spread to the central nervous system, the natural immunity failed completely. The development of a second infection, for instance the concurrence of diphtheria and measles, may lead to such a complete failure of the natural immunity. The author further reports the history of a child, who, because the first vaccination against smallpox had not taken, was revaccinated, and this time the vaccinia presented the usual aspects. About the time when the formation of the immune bodies had already passed its peak, the child developed whooping cough, which took an especially severe course. This second infectious disease influenced the immunization processes against vaccinia so unfavorably that the immunity was practically lost again. The vaccination scar developed a new reaction. Later the immunity processes became active again and the child recovered. The author points out that in the Spanish literature the suggestion has been made to employ smallpox vaccination for the treatment of whooping cough, but that some Spanish authors have objected to this method. He thinks that his case, in which whooping cough and vaccinia accidentally concurred, is an argument against that treatment, because the severe course of the whooping cough was the result of the smallpox vaccination that had preceded it.

Roentgenoscopy in Diagnosis of Appendicitis.—Kleinschmidt describes his experiences with roentgenoscopy of the appendix in a number of children. He reaches the conclusion that roentgenoscopy with the aid of contrast filling is not suited for the diagnosis of appendicitis. He found that the evacuation time differs widely even in normal appendixes, and he thinks that it is largely determined by anatomic and physiologic peculiarities, such as the length, position and lumen of the appendix, the intestinal activity and the mode of life. At any rate, the isolated filling of the appendix may last 100 hours and even more when the organ is healthy, so that a filling that lasts this length of time need not be indicative of a pathologic condition. If filling does not take place, an obstruction of the lumen of the appendix exists, which may be in the nature of mechanical factors (fecal concretion, fixation or bending), of inflammatory changes (swelling of the mucous membrane) or of severe contraction of the musculature of the antrum. A diseased appendix may prevent filling partly or completely or may cause an unusually prolonged filling. Differences in the duration of the filling of the cecum and the appendix are unsuited for the diagnosis of a disorder of the appendix. The author was unable to corroborate the statement that the evacuation time becomes normalized after the inflammation of the appendix has subsided.

Zentralblatt für Gynäkologie, Leipzig

58: 2881-2944 (Dec. 8) 1934

*Reactivation of Senile Human Ovaries. L. Waldeyer.—p. 2882.
*Cystic Tumor of Sublingual Gland and Pregnancy. R. Luh.—p. 2891.
Experience with Cancer Reaction According to Fuchs. F. Friedl and E. Kulka.—p. 2896.
Statistical Studies on Dependence of Female Fertility on Age. H. Münzner and K. Löer.—p. 2900.
Internal Endometriosis in Form of Unusually Large Solitary Chocolate Cyst. M. Mátyás.—p. 2903.
Marking of the New-Born for Purpose of Preventing Mistakes in Identity. F. Kovács.—p. 2908.

Reactivation of Senile Human Ovaries.—Waldeyer points out that Zondek and Aschheim and several other investigators succeeded in bringing about regular estrus in old animals by the administration of the hormone of the anterior hypophysis. Attempts were made by Tschertok and Penkow and by Westman to reactivate senile human ovaries by injecting urine or blood from pregnant women. In order to be able to determine the efficacy of the experiment they gave these injections to women of the menopausal age, who had to undergo operations on the genitalia. Tschertok and Penkow employed pregnancy urine and obtained negative results in all except one of the cases, and in this one estrogenic substance had been administered in addition to the urine. Westman, who used pregnancy blood in two cases, observed what he considered a reactivation of the ovaries, and he concludes from this that it is possible to reactivate the ovaries of women of the menopausal age by injecting the sex hormone of the anterior lobe of the hypophysis. The author thinks that a number of his observations can serve as controls of Westman's experiments, for he examined the ovaries of women of the menopausal age without previous injection of gonadotropic substances. Observations in seven cases convinced him that the development of a follicle to the stage of a young corpus luteum, together with the corresponding changes in the uterine mucous membrane, can take place during the menopause, although no hormone has been administered. Moreover, he points out that Robert Meyer observed even a fully developed corpus luteum. The author concludes that he does not care to deny the possibility of a modification of the resting follicles in the ovaries of women of the menopausal age, but he wants to point out that great precaution is necessary

in the evaluation of experiments on the action of the gonadotropic hormone of the hypophysis on human ovaries.

Tumor of Sublingual Gland and Pregnancy.—Luh thinks that pathologic changes of a morphologic nature in the salivary glands, during or as the result of pregnancy, are rare. He admits that more than two decades ago certain relations were detected between changes in the salivary glands and the genital organs, but a causal connection was not discovered. Even the ptyalism of pregnancy has as yet found no causal explanation. Madruzza made studies on pregnant rats and mice and found the interstitial tissues of the salivary glands unchanged but noted that the acini of the parotid and submaxillary glands were in a state of increased function, while those of the sublingual gland were at rest. The excessive enlargement or swelling of one or the other of the salivary glands during pregnancy is extremely rare and for this reason the author feels justified in reporting the case of a woman who gave birth to a normal girl and who had a tumor in the anterior portion of the neck. The growth reached from the region of the thyroid cartilage to the third rib and was oval. Palpation indicated that the growth was a slightly fluctuating cyst. A cone-like process about 10 cm. in length branched off from the main tumor in the direction of the submaxillary angle. Pressure on the tumor resulted in a swelling of the branch directly below the submaxillary angle. The entire submental region was lowered in the form of a double chin. Inspection of the oral cavity disclosed a transparent, cystic growth in the region of the sublingual caruncle. There seemed to be no communication between the tumor in the neck and this cyst. The tumor of the neck remained unchanged during the period of expulsion of the fetus. Until the anamnesis was taken, it seemed that there was no connection between the tumor and gestation. The woman stated that her first pregnancy terminated in the sixth month, the fetus being dead. On the third day following the abortion, a tumor developed in the mouth and became so large that she could be fed only fluids introduced by means of a tube. On the fifteenth day following the abortion, the physician punctured this tumor and a watery fluid was discharged. The patient recovered completely, the growth having entirely disappeared. At about the middle period of the second pregnancy, which was carried to term, a tumor formed at the right submaxillary angle and the floor of the mouth felt somewhat elevated. During the puerperal period the tumor as well as the swelling of the floor of the mouth disappeared, but later the woman noticed that during the menstrual periods the swellings returned in a milder form and then disappeared again. At the end of the third month of the third pregnancy she observed the reappearance of the swelling at the submaxillary angle and on the floor of the mouth and shortly after that the tumor formed in the anterior part of the neck. This anamnesis reveals the close connection between pregnancy and the development of the tumors. One month after the termination of the third pregnancy, the tumor was punctured. The contents, a jelly-like substance about 90 Gm. in weight, were examined. Shortly after that the cyst was likewise removed and examined. Although the examinations revealed neither a neoplasm nor an inflammatory tumor, it must nevertheless be assumed that the tumor developed on the basis of a chronic interstitial inflammation with subsequent retention of the secretion.

Klinischeskaya Meditsina, Moscow

12: 1395-1520 (Nov. 10) 1934. Partial Index

Use of Histamine in Therapy of Various Diseases. A. O. Frayfeld.—p. 1418.
Atypical Forms of Ulcer Disease and Their Diagnosis. I. M. Flekel and B. M. Shtern.—p. 1427.
Pathogenesis and Basic Principles of Treatment of Peptic Ulcers. G. Ya. Gurevich.—p. 1434.
Roentgen Therapy of Ulcer of Stomach and Duodenum. L. L. Golst, G. Shal and N. P. Negovskiy.—p. 1442.
Id. L. F. Gorina, P. S. Fass and L. N. Fedorova.—p. 1453.
Significance of Immunity and Anaphylaxis in Chronic Infectious Colitis. L. B. Berlin, O. O. Schmidt and B. S. Levin.—p. 1460.
*Pathogenesis of Gout. I. A. Golyanitskiy.—p. 1477.

Pathogenesis of Gout.—Golyanitskiy says the experimental production of gout has not been accomplished. Clinical observation still remains the main source of information in the malady. Visceral gout is frequently observed in chickens and in hens. The essential pathologic characteristics of gout in birds and associated renal and hepatic lesions suggest a similarity with gout in man, although the process cannot be viewed as identical. Atmospheric conditions and temperature play an important part in the pathogenesis of gout, and dietetic regimen plays an even greater part. The significance of the various components of the diet, such as albumins, carbohydrates, fats and minerals, may be positive or negative depending on varying conditions. Deficiency in vitamins, minerals or ferments with the associated acidosis may act as the deciding factor. Prophylaxis of gout should be directed toward a favorable alteration of the enumerated factors and toward combating acidosis. The therapy should be many sided and, besides the diet, should utilize all the means of increasing the oxidating processes and of raising the alkali reserve.

Nederlandsch Tijdschrift voor Geneeskunde, Haarlem

78: 5805-5864 (Dec. 29) 1934

Discussion of Hyperemesis of Pregnancy. C. J. H. de Geus.—p. 5812.
*Anatomopathology of Psittacosis in Man. B. J. Mansens.—p. 5818.
Hutchinson's Teeth in Upper Jaw and Pflüger's Molars in Lower Jaw: Case. T. E. de Jonge-Cohen.—p. 5829.
Mesentery Fibroma: Case. J. Van Der Spek.—p. 5833.

Pathology of Psittacosis in Man.—Mansens reviews the conditions that have been described in the organs of man in psittacosis and presents a new case of the disease with photomicrographs. The typical psittacotic lung is characterized by a lobular confluent pneumonia. The cut surface is gray or red, smooth and moist, but not granular. There is a highly varying exudate, which may consist of a serous fluid, generally with little fibrin, many or few large mononuclear cells, and few leukocytes. Undoubtedly the large cells are partly desquamated cells of the alveolar lining, and partly macrophages. The interstitium may be thickened. The pleurae may have a light fibrinous membrane, but most frequently they are smooth. The bronchi are often empty or contain only a serous exudate with little cells. The author attributes the predominance of leukocytes to secondary infections, which commonly occur. The liver and the kidney show epithelial degeneration. Sometimes focal necrosis is seen in the liver. The reticulo-endothelial system of the spleen is swollen; the same may occur in the liver. In several organs, hemorrhages may be observed. The author concludes that, whereas the pathologic picture of psittacosis supports its diagnosis, it is not sufficiently specific to replace the clinical and epidemiologic picture.

Norsk Magasin for Lægevidenskapen, Oslo

95: 1361-1464 (Dec.) 1934

*Number of Infections with Streptococcus Epidemicus Together with Biochemical and Serologic Investigations of Properties of This Microbe. T. Thjøtta and S. D. Henriksen.—p. 1361.
Influence of Magnesium Salts on Development of Tar Tumors in Mice. L. Kreyberg and S. S. Nielsen.—p. 1389.
Did Sigurd Jorsalfar Allow Necropsy of One of His Men in Byzantium? F. Grøn.—p. 1405.
Features of Earlier History of Rickets. I. Reichborn-Kjennerud.—p. 1419.
Isolated Traumatic Fracture of Symphysis: Two Cases. T. Lillejord.—p. 1436.
Pes Excavatus. E. Moen.—p. 1441.
Investigations on Occurrence of Microbes in Some Alcohol Specimens. K. Hansen and E. Blegen.—p. 1448.

Infections with Streptococcus Epidemicus.—In twenty-two cases of infections due to Streptococcus epidemicus during the winter of 1933-1934, Thjøtta and Henriksen found that the microbe was in all respects identical with the Streptococcus epidemicus described by Davis and Rosenow in 1912. Biochemically the strains were uniform; all were human strains. Serologically slight differences, demonstrable only by absorption and agglutination, appeared between the strains from Oslo-Aker and the three Røros. The strains are all ascribed to the same source of infection, which, however, was not confirmed. Clinically the cases ranged from more or less severe inflammations of the skin to septic sore throat, erysipelas, bronchopneumonia and sepsis; four cases were fatal. Comparison between these strains and the angina streptococcus from the epidemic of milk-borne septic sore throat in Oslo in 1908 described by Ustvedt and investigated by Holth indicates that the microbes from 1908 and from 1934 are of the same type.